

FIG. 6

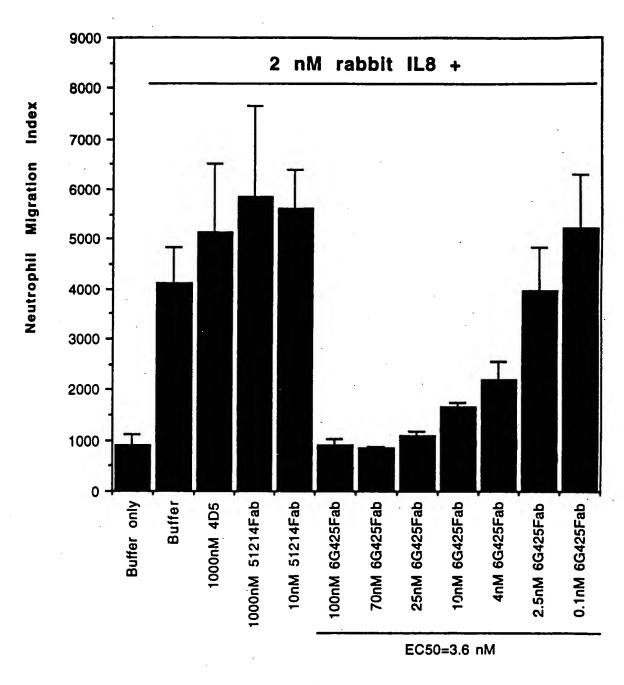
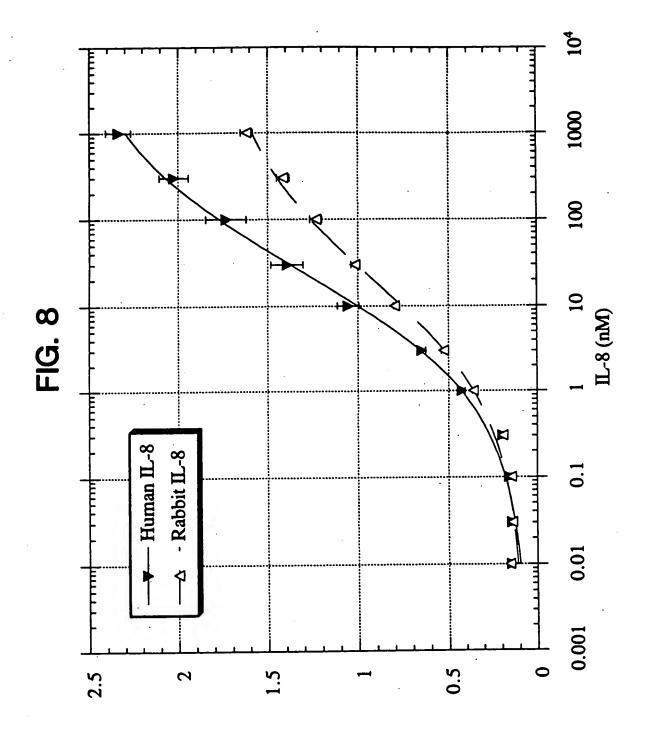


FIG. 7

Absorbance (405 nm)

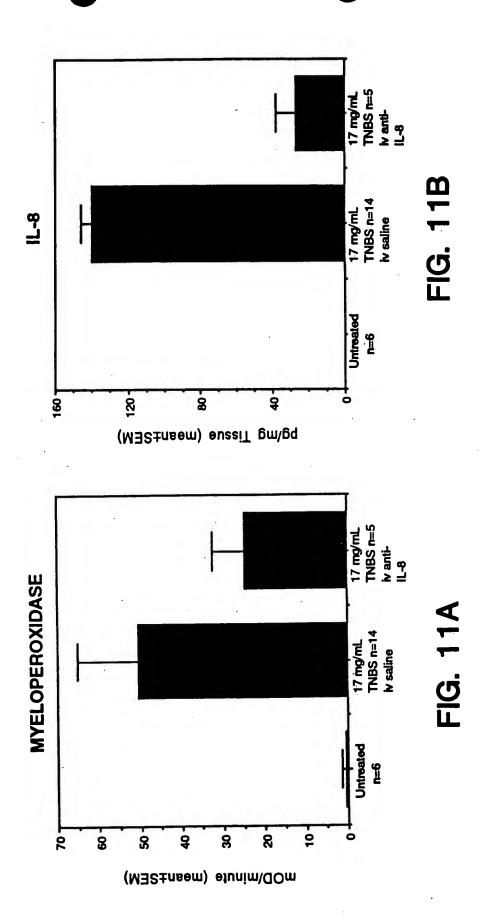


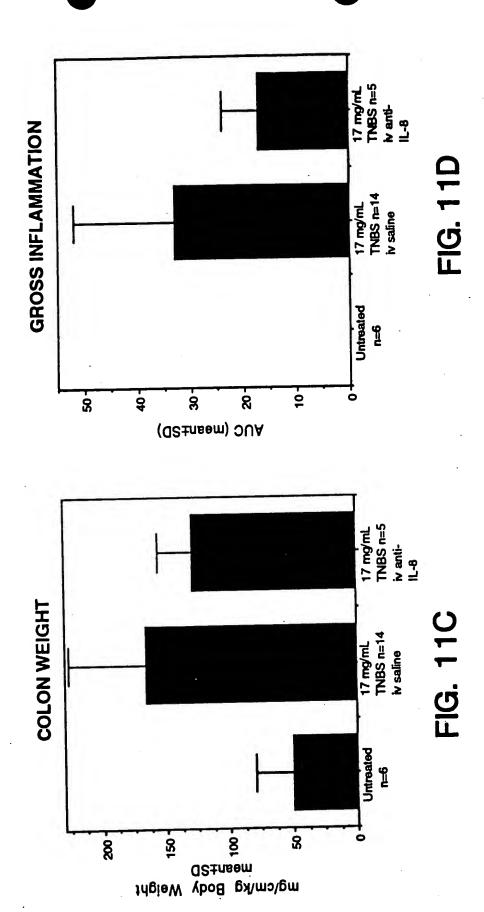
- A51214 + 100 nM IL-8 - - 6G425 + 100 nM IL-8 10 100 nM IL-8 Alone . 9 · - 4D5 + 100 nM IL-8 A51214 Alone 6G425 Alone 4D5 Alone X B Molar Ratio Fab: IL-8 FIG. 9 0.99536 0.6428 0.99813 0.6351 6G425 A51214 IC50 ICS0 9 9 20 0 120 80 100

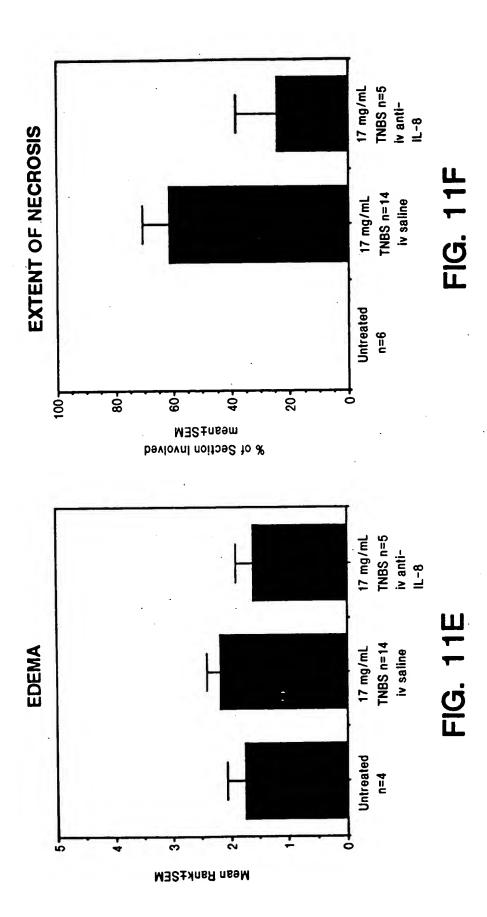
% IL-8-Stimulated Elastase Release

2 1.0401 0.99539 6G425 X 4P Fit IC50 2 Molar Ratio Fab:rIL-8 FIG. 10 - A51214 + 100 nM rIL-8 - - 6G425 + 100 nM rIL-8 - . ө · - 4D5 + 100 nM rIL-8 100 nM rIL-8 Alone A51214 Alone 6G425 Alone 4D5 Alone æ × 0 0.2 9.0 0.8

Absorbance (405 nm)







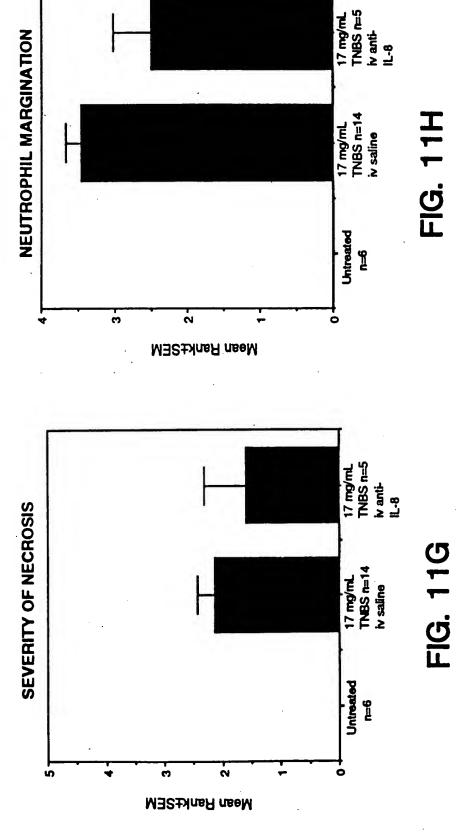
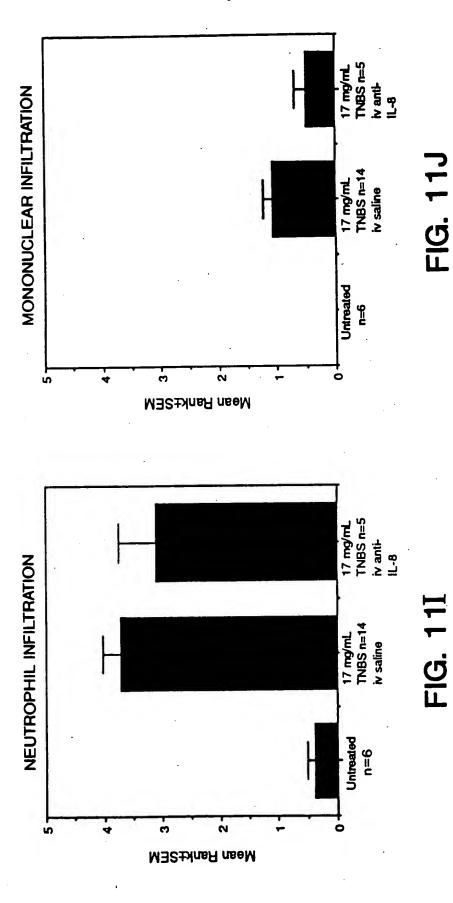
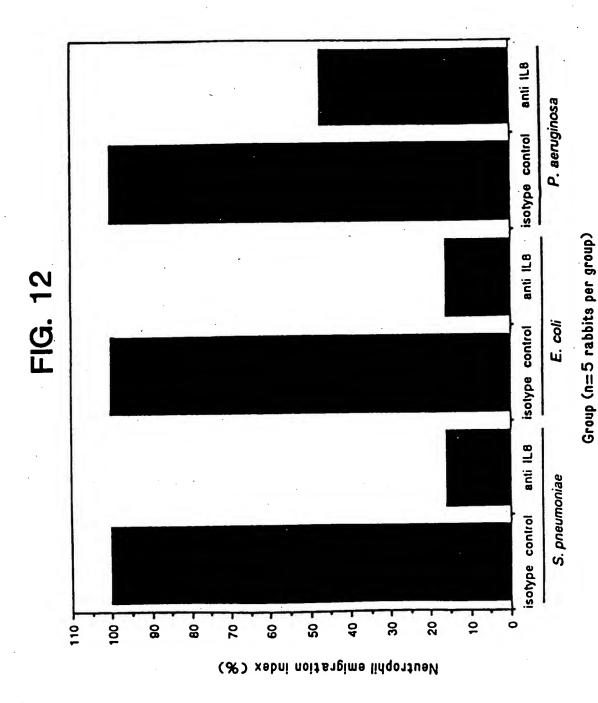


FIG. 11H





## Light Chain Primers: FIG. 13 MKLC-1, 22mer 5' CAGTCCAACTGTTCAGGACGCC 3' MKLC-2, 22mer 5' GTGCTGCTCATGCTGTAGGTGC 3' MKLC-3, 23mer 5' GAAGTTGATGTCTTGTGAGTGGC 3 ' Heavy Chain Primers: IGG2AC-1, 24mer י 3 5 GCATCCTAGAGTCACCGAGGAGCC IGG2AC-2, 22mer 5' CACTGGCTCAGGGAAATAACCC 3' IGG2AC-3, 22mer 5' GGAGAGCTGGGAAGGTGTGCAC 3'

## FIG. 14

Light chain forward primer

SL001A-2 35 mer

5' ACAAACGCGTACGCT GACATCGTCATGACCCAGTC 3'

r r A

Light chain reverse primer

SL001B 37 mer

5' GCTCTTCGAATG GTGGGAAGATGGATACAGTTGGTGC 3'

Heavy chain forward primer

FIG. 15

SL002B 39 mer

5' CGATGGGCCCGG ATAGACCGATGGGGCTGTTGTTTTGGC 3'

T

G

Α

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCGG ATAGACCGATGGGGCTGTTGTTTTGGC 3

 ${f T}$ 

A

G.

- CTGTAACAGT ACTGTGTCAG AGTTTTTAAG TACAGGTGTA GTCATCCTCT GTCCCAGTCG 1 GACATTGTCA TGACACAGTC TCAAAAATTC ATGTCCACAT CAGTAGGAGA CAGGGTCAGC Ŋ Ø
- 61 GTCACCTGCA AGGCCAGTCA GAATGTGGGT ACTAATGTAG CCTGGTATCA ACAGAAACCA CAGTGGACGT TCCGGTCAGT CTTACACCCA TGATTACATC GGACCATAGT TGTCTTTGGT Ø X M > Z \* CDR #1 N \* 0 **A** \* . K 21 V
- 121 GGGCAATCTC CTAAAGCACT GATTTACTCG TCATCCTACC GGTACAGTGG AGTCCCTGAT TCAGGGACTA > CCCGTTAGAG GATTTCGTGA CTAAATGAGC AGTAGGATGG CCATGTCACC CDR #2 Ŋ \* S н
- ACACGTCAGA 181 CGCTTCACAG GCAGTGGATC TGGGACAGAT TTCACTCTCA CCATCAGCCA TGTGCAGTCT GCGAAGTGTC CGTCACCTAG ACCCTGTCTA AAGTGAGAGT GGTAGTCGGT ഗ E Ω Ŋ
- 241 GAAGACTTGG CAGACTATTT CTGTCAGCAA TATAACATCT ATCCTCTCAC GTTCGGTCCT CTTCTGAACC GTCTGATAAA GACAGTCGTT ATATTGTAGA TAGGAGAGTG CAAGCCAGGA Œ T Z CDR ø ပ
- 301 GGGACCAAGC TGGAGTTGAA ACGGGCTGAT GCTGCACCAC CAACTGTATC CATCTTCCCA GTAGAAGGGT TGCCCGACTA CGACGTGGTG GTTGACATAG ۵ Д Ω ď CCCTGGTTCG ACCTCAACTT × E ტ

BstBI 361 CCATTCGAA GGTAAGCTT

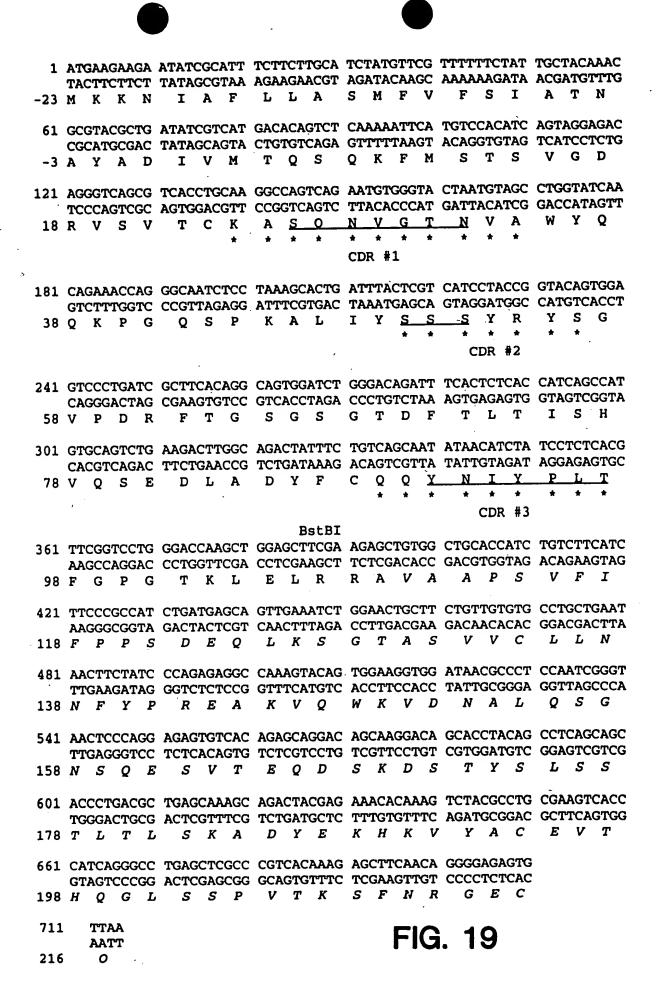
PF

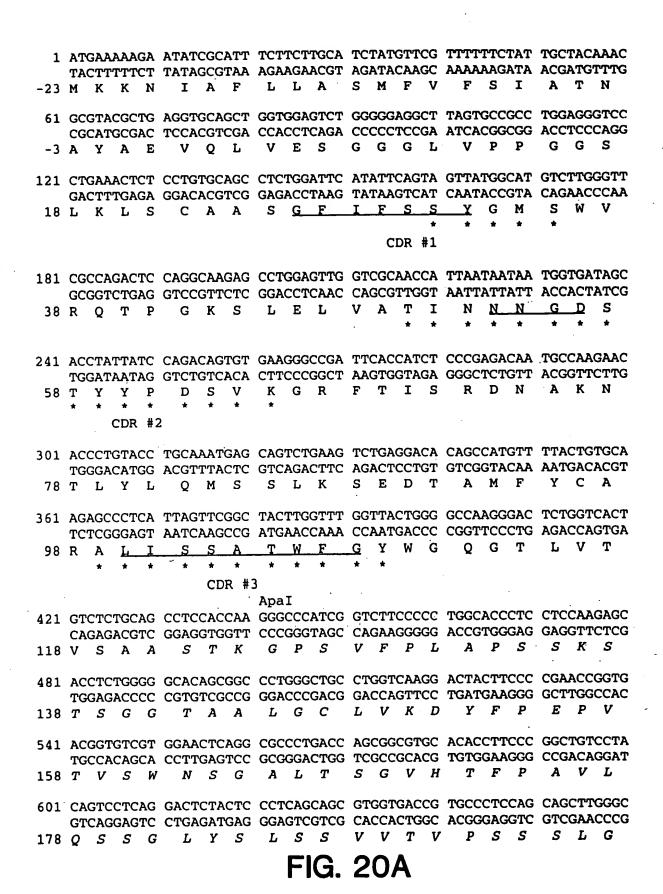
121

F. 7

1	ጥጥርጥልጥጥርርጥ	ACAAACGCGT	<b>АСССТСАССТ</b>	GCAGCTGGTG	GAGTCTGGGG	GAGGCTTAGT
•					CTCAGACCCC	
1			E V	QLV	E S G G	G L V
. 61					GGATTCATAT	
	CGGCGGACCT	CCCAGGGACT	TTGAGAGGAC		CCTAAGTATA	AGTCATCAAT
13	P P G	G S L K	L S C	A A S	G F I F	S S Y
	•	•				. * *
					- CDR	<b>#1</b> .
101	maaaa mamam	maaammaaaa	ACACMCCACC	CARCACCCTC	CACMMCCMCC	CAACCAMMAA
121					GAGTTGGTCG CTCAACCAGC	
. 33	G M S	W V R O			E L V A	T I N
33	4 * *	WVKQ	I P G	K 5 D	E D V A	* * *
181	TAATAATGGT	GATAGCACCT	ATTATCCAGA	CAGTGTGAAG	GGCCGATTCA	CCATCTCCCG
					CCGGCTAAGT	
53	N N G	D S T Y	Y P D	s v K	G R F T	I S R
	* * *	* * * *	* * *	* * *		
		CDR #2	2			
241					CTGAAGTCTG	
				•	GACTTCAGAC	
73	D N A	K N T L	Y L Q	M S S	L K S E	DTA
301	<u> </u>	TGTGC A AGAG	СССТСАТТАС	ттсссстаст	TGGTTTGGTT	ACTGGGGCCA
301					ACCAAACCAA	
.93		C A R A		SAT	W F G Y	WGQ
		*	* * *	* * *	* * * *	
			CI	OR #3		
361	AGGGACTCTG					
		CAGTGACAGA				
113	G T L	V T V S	A A K	TTA	P S V Y	
	<b>&gt;</b>					
411	ApaI ATCC <i>GGG</i>					
411	TAGGCCC		-		-10 47	
130	P			· •	FIG. 17	
150	E			_		

VL.front	31-MER		
5' ACAA <u>ACGCGT</u> VL.rear 31-ME	ACGCT <u>GATATC</u> GTCATGACAG R	3'	
5 GCAGCATCAG	CTC <u>TTCGAA</u> GCTCCAGCTTGG	3'	
VH.front.SPE	21-MER	٠	
5' CCACTAGTAC	GCAAGTTCACG	3 ' ·	
VH.rear 33-ME	R		
5' GATGGGCCCT	TGGTGGAGGCTGCAGAGACAGT	G .	3





- 661 ACCCAGACCT ACATCTGCAA CGTGAATCAC AAGCCCAGCA ACACCAAGGT GGACAAGAAA TGGGTCTGGA TGTAGACGTT GCACTTAGTG TTCGGGTCGT TGTGGTTCCA CCTGTTCTTT 198 T Q T Y I C N V N H K P S N K V D K K
- 721 GTTGAGCCCA AATCTTGTGA CAAAACTCAC ACATGA CAACTCGGGT TTAGAACACT GTTTTGAGTG TGTACT

K T H218 V E P K S C D

**FIG. 20B** 

Light Cl	nain Primers:	
MKLC-1,	22mer	
5'	CAGTCCAACTGTTCAGGACGCC 3'	
MKLC-2,	22mer	
5'	GTGCTGCTCATGCTGTAGGTGC 3'	,
MKLC-3,	23mer	
5'	GAAGTTGATGTCTTGTGAGTGGC	3 '
	nain Primers: 1, 24mer	
5 <sup>1</sup>	GCATCCTAGAGTCACCGAGGAGCC	3 '
IGG2AC-2	2, 22mer	
5'	CACTGGCTCAGGGAAATAACCC 3'	
IGG2AC-	3, 22mer	
5 †	GGAGAGCTGGGAAGGTGTGCAC 3'	
	FIG. 21	

Light chain forward primer

6G4.light.Nsi 36-MER

5' CCAATGCATACGCT GAC ATC GTG ATG ACC CAG ACC CC 3'
T T T T
A A

Light chain reverse primer

6G4.light.Mun 35-MER

5' AGA TGT CAA TTG CTC ACT GGA TGG TGG GAA GAT GG 3'

Heavy chain forward primer

6G4.heavy.Mlu 32-MER

5' CAAACGCGTACGCT GAG ATC CAG CTG CAG CAG 3'

T C

Heavy chain reverse primer

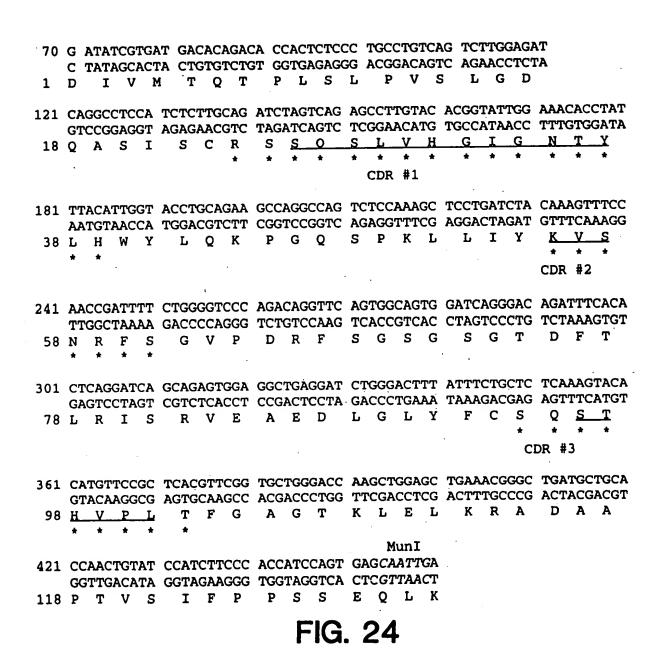
\$L002B 39-MER

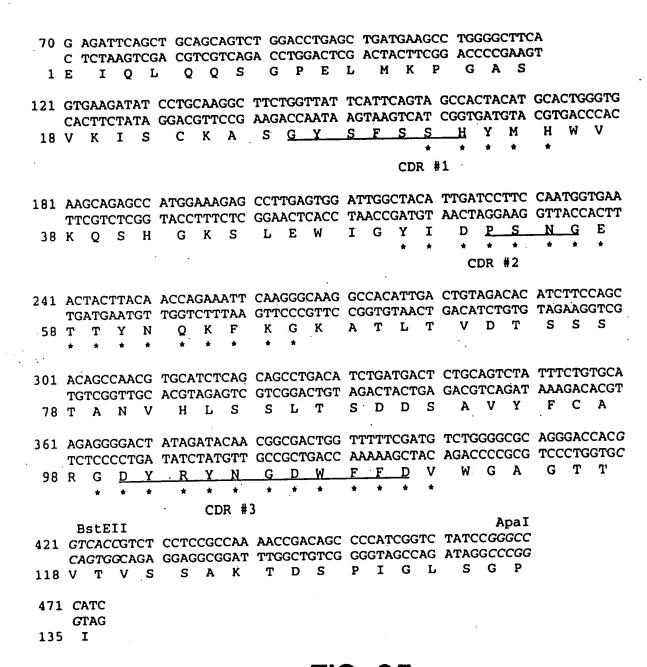
5' CGATGGGCCCGG ATAGACCGATGGGGCTGTTGTTTTGGC 3

T
A

FIG. 23

G





5' CTTGGTGGAGGCGGAGGAGACG 3'

Mutagenesis Primer for 6G425VL

DS/VF 38MER

5' GAAACGGGCTGTTGCTGCACCAACTGTATTCATCTTCC 3'

SYN.BstEII 31 MER

5' GTCACCGTCT CCTCCGCCTC CACCAAGGGC C 3'

SYN.Apa 22 MER

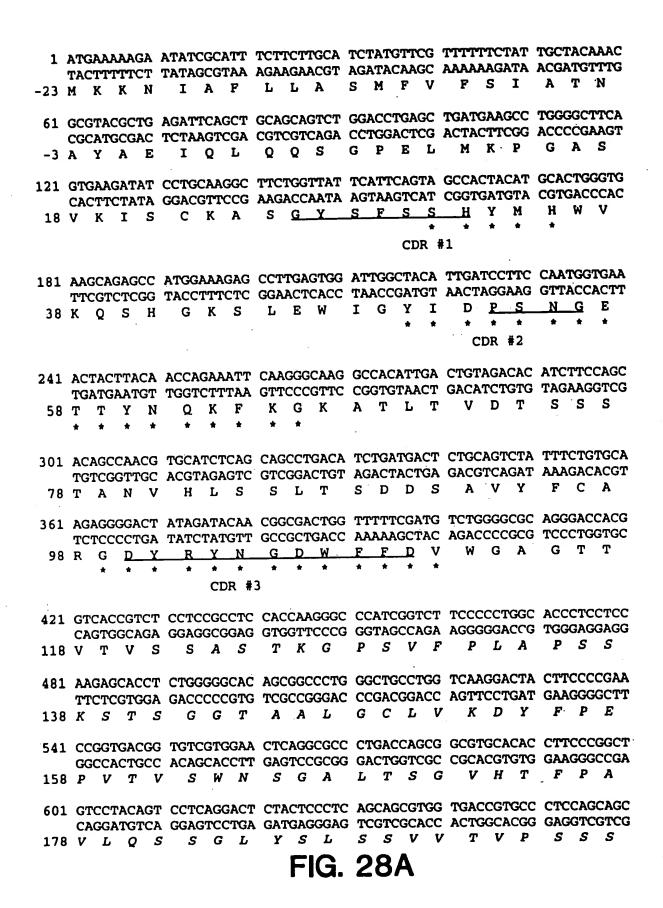
5' CTTGGTGGAGGCGGAGACG 3'



**FIG. 27A** 

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTTCTCGAA GTTGTCCCCT  $A \ C \ E \ V \ T \ K \ S \ F \ N \ R \ G$ G L T H Q 198

721 GAGTGTTAA CTCACAATT 218 E C O FIG. 27B



AACCCGTGGG TCTGGATGTA GACGTTGCAC TTAGTGTTCG GGTCGTTGTG GTTCCACCTG 661 TTGGGCACCC AGACCTACAT CTGCAACGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC KV S Д × N H CNV T 198 L G

721 AAGAAAGTTG AGCCCAAATC TTGTGACAAA ACTCACACAT GA TTCTTTCAAC TCGGGTTTAG AACACTGTTT TGAGTGTGTA CT 218 K K V E P K S C D K T H T O

FIG. 28B

## Variable Light Chain Domain

	10 20 abcde 30 40
6G425	10 20 abcde 30 40 DIVMTQTPLSLPVSLGDQASISCRSSQSLVHGIGNTYLHWYLQKPGQSPKLLIY
00.20	# # # ## # ### # # ##
F(ab)-1	DIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTYLHWYQQKPGKAPKLLIY
humĸI	DIQMTQSPSSLSASVGDRVTITCRASKTISKYLAWYQQKPGKAPKLLIY
	.1.1
	<del></del>
	50 60 70 80 90 100
6G425	YKVSNRFSGVPDRFSDSGSGTDFTLRISRVEAEDLGLYFCSQSTHVPLTFGAGTKLELKR
777 1 3 4	# # # ################################
F(ab)-1	YKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPLTFGQGTKVEIKR ## ###
haranay.	YSGSTLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQHNEYPLTFGQGTKVEIKR
humĸI	A2G24FF2GA62G2G4D44F41122F64F544114C66444F4444
	++++++
	L2 L3
	Variable Heavy Chain Domain
	10 20 30 40
6G425	EIQLQQSGPELMKPGASVKISCKASGYSFSSHYMHWVKQSHGKSLEWI
	# ## ## ## # # ## # #
F(ab)-1	EVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMHWVRQAPGKGLEWV
humIII	# ## # # EVQLVESGGGLVQPGGSLRLSCAASGFSFTGHWMNWVRQAPGKGLEWV
HUIIIII	E4504 F2669 F461 G02 TV TO CONTINUE TO CON
	*****
	H1
,	50 a 70 80 abc 90 100 110
6G425	50 a 70 80 abc 90 100 110 GYIDPSNGETTYNQKFKGKATLTVDTSSSTANVHLSSLTSDDSAVYFCAARGDYRYNGDWFFDVWGAGT
00423	## ### # ## ### # ## ## ## #
F(ab)-1	GYIDPSNGETTYNQKFKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAARGDYRYNGDWFFDVWGQGT
_ (, -	* * * * * * * * * * * * * * * * * * * *
humIII	GMIHPSDSETRYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAARGIYFY-GTTYFDYWGQGT
	++++++++++++++++++++++++++++++++++++++
	H2

FIG. 29

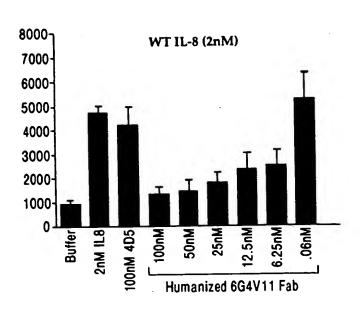


FIG. 30A

IC50~12nM

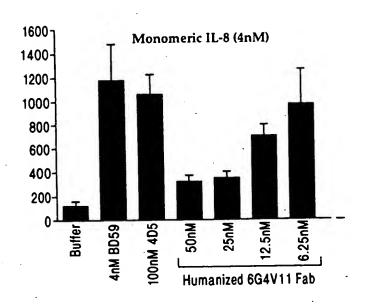


FIG. 30B

IC50~15nM

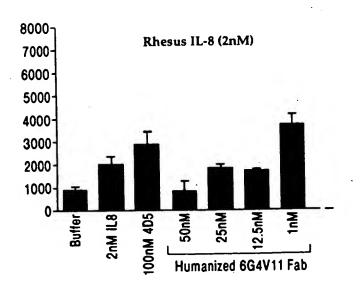


FIG. 30C

IC50~22nM

# Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Light Chain

LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQST HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLINNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTY

## anti-IL-8 6G4.2.5V11 Heavy Chain Amino Acid Sequence of the humanized

WVRQAPGKGLEWVGYIDPSNGETTYNQKFKGRFT**L**SRDNSKNT**A**YLQMNSLRAEDTAVYY CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK MKKNIAFLLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH VDKKVEPKSCDKTHT

## Amino Acid Sequence of the peptide linker and M13 Phage Coat (gene-III)

SGGGSGSGDFDYEKMANANKGAMTENADENALQSDAKGKLDSVATDYGAAIDGFIGDVS **GLANGNGATGDFAGSSNSQMAQVGDGDNSPLMNNFRQYLPSLPQSVECRPFVFSAGKPY** EFSIDCDKINLFRGVFAFLLYVATFMYVFSTFANILRNKES

## FIG. 31A

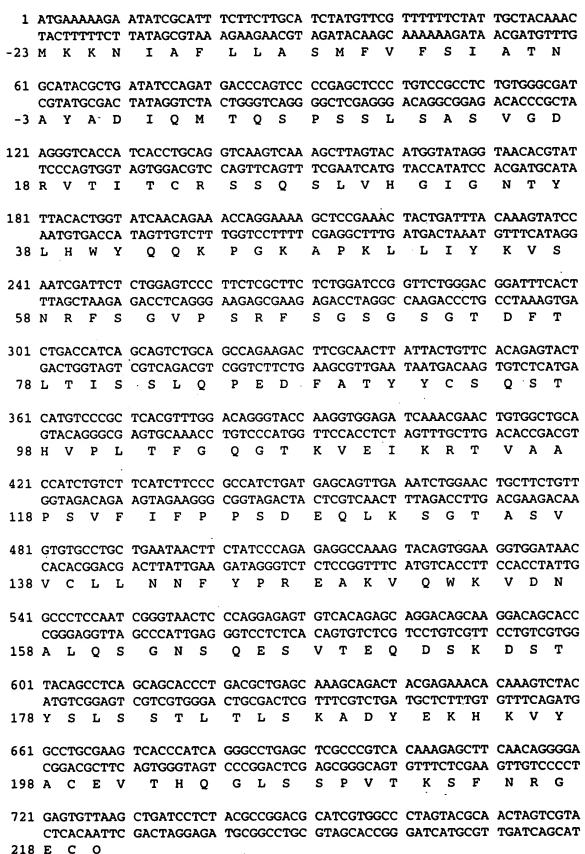


FIG. 31B

### Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Light Chain

ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQST HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTY

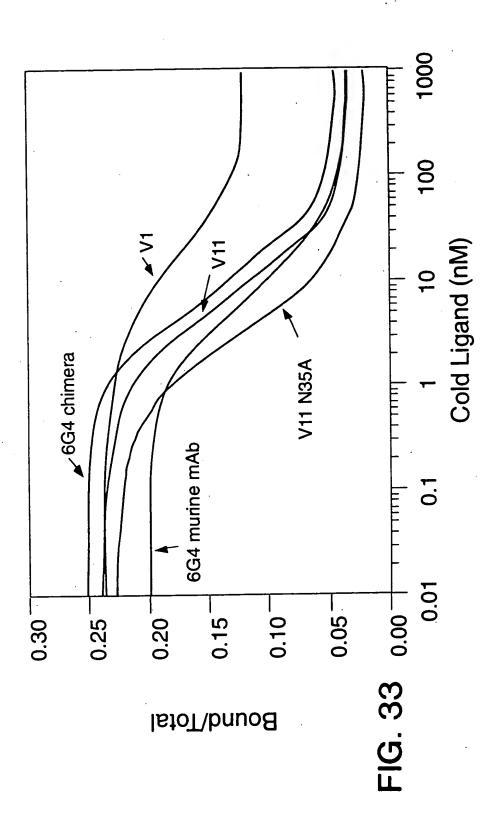
## Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Heavy Chain

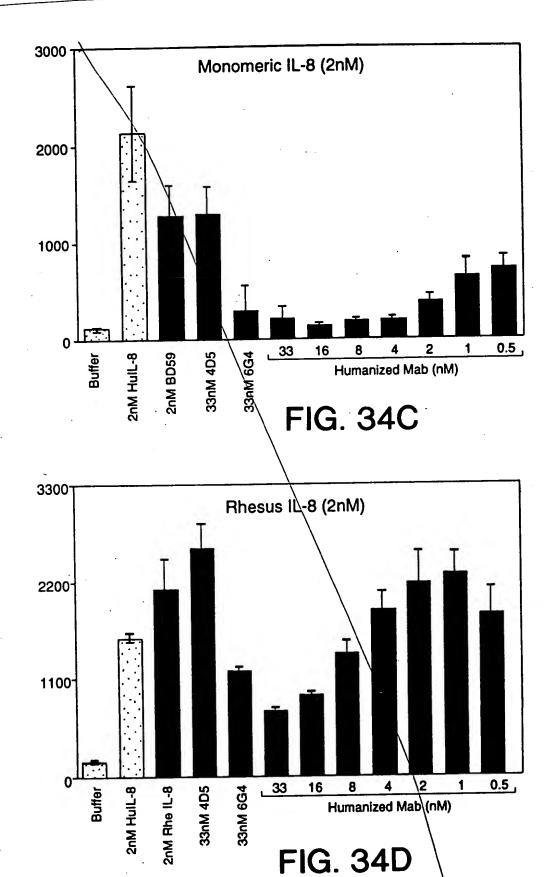
WVKQ**a**pgkglewvgyidpsngettynokfkgrft**l**srdnsknt**a**ylomnslraedtavyy CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK MKKNIAFLLASMFVFSIATNAYAEVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMH VDKKVEPKSCDKTHT

#### -1G. 31C



F16.32





### anti-IL-8 6G4.2.5V11N35A Light Chain Amino Acid Sequence of the humanized

LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQST HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN **ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG** MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIG**A**TY

# Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Heavy Chain

**WVRQAPGKGLEWVGYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF** PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK MKKNIAFLLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH VDKKVEPKSCDKTHT Amino Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper

CPPCPAPE<u>LL</u>GGRMKQLEDKVEELLSKNYHLENEVARLKKLVGER

**-1G.** 35

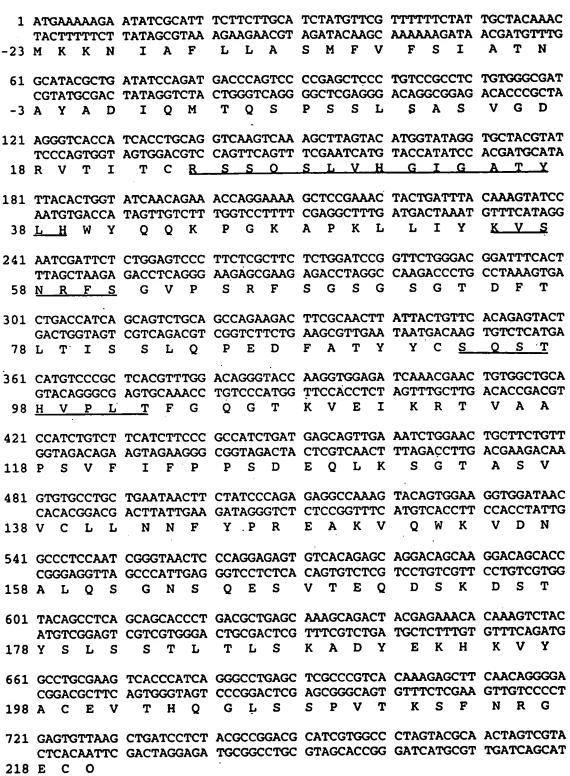
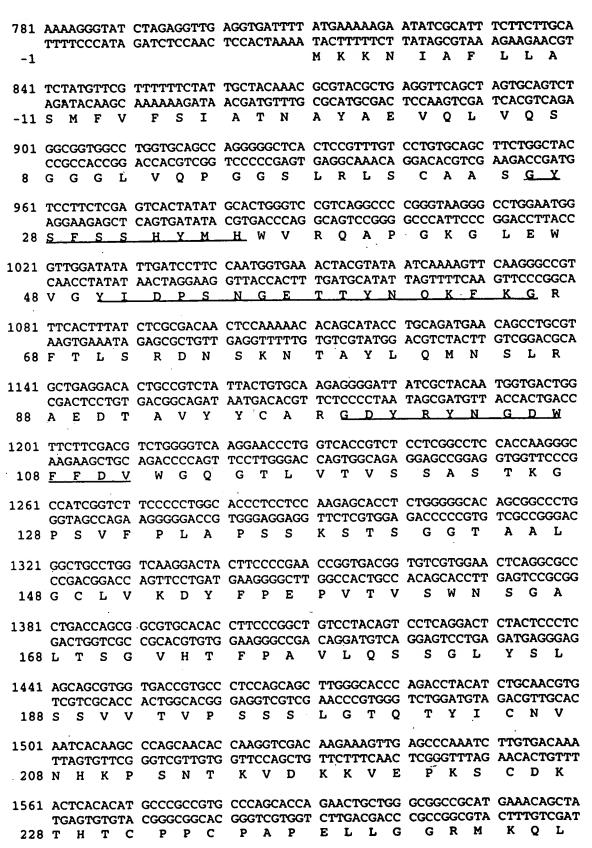


FIG. 36

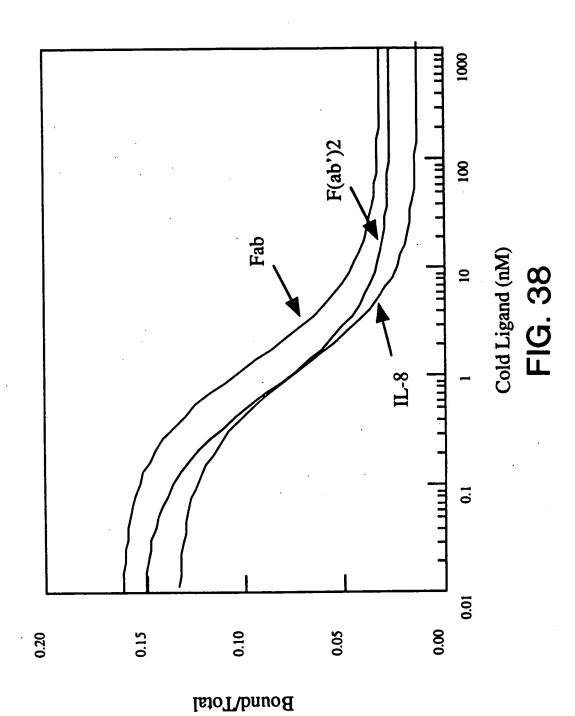


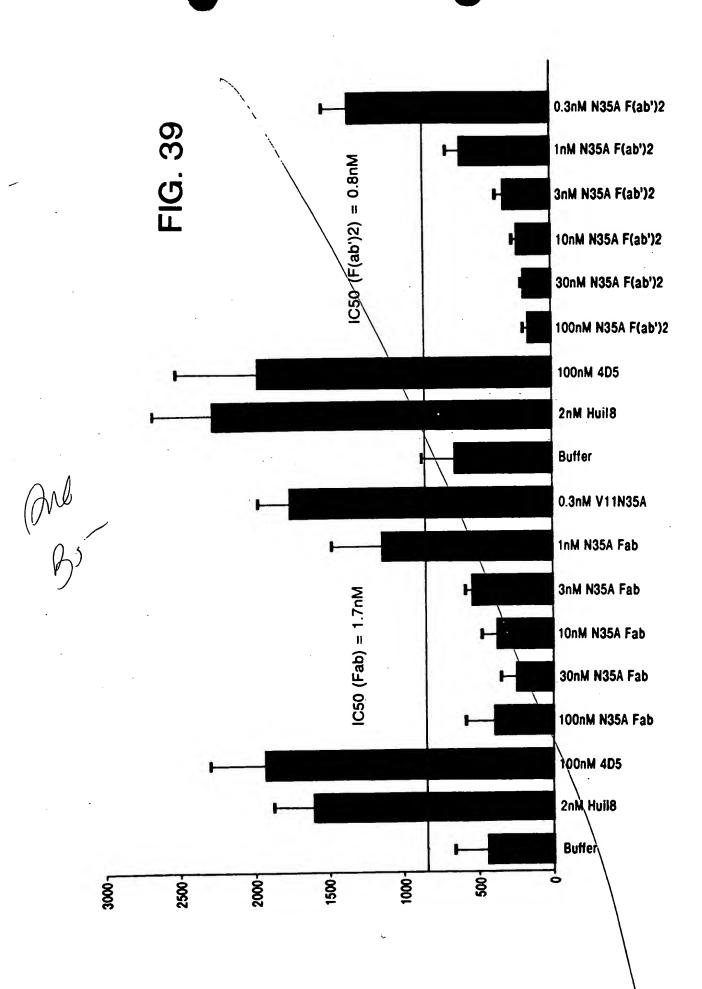
**FIG. 37A** 

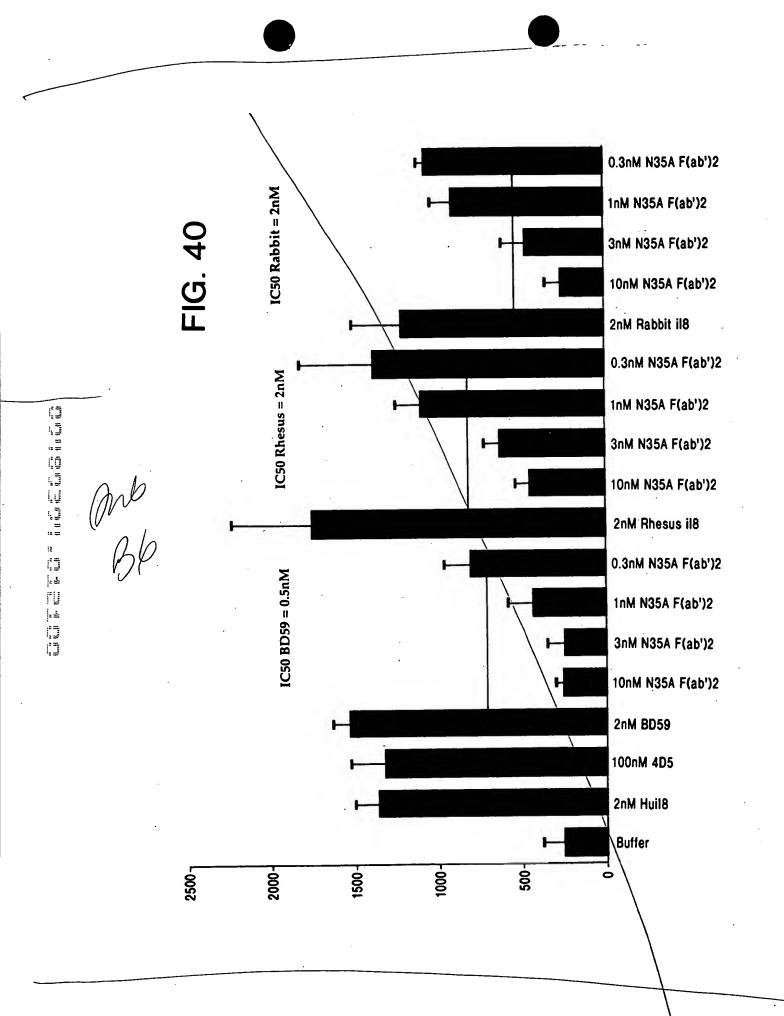
1621 GAGGACAAGG TCGAAGAGCT ACTCTCCAAG AACTACCACC TAGAGAATGA AGTGGCAAGA CTCCTGTTCC AGCTTCTGA TGAGAGGTTC TTGATGGTGG ATCTCTTACT TCACCGTTCT 248 E D K V E E L L S K N Y H L E N E V A R

1681 CTCAAAAAGC TTGTCGGGGA GCGCTAA GAGTTTTTCG AACAGCCCCT CGCGATT 268 L K K L V G E R O

FIG. 37B







alui plei hindili mboli taqi 91 earl/kap6321 I. cac81 mboli hinfi AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT	sau3AI mbol/ndeII[dam-] dpnI[dam+] acii dpnII[dam-] nspBII bclI[dam-] ACCAACAGGG GTTGATTGAT CAGGTAGAGG	mbli foki sfani aaagaagta ctcgtcagta tttcttcaat aacttcgtag gagcagtcat	alui sali sati saci hqiJII hqiJII hqiJII ecoli36II ecil36II mael bsp1286 rmal bsiHKAI mael bmyI msel maeli apoi banii TTTTAATGTA TTTGTAACTA GAATTCGAGC AAAATTACAT AAACATGAT CTTAAGCTCG
ddel tru nlaIII bsrDI AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT TTTATGTCTG TACTTTTTAG AGTAACGACT CAACAATAAA	msli maeili bsrbi ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG TAATAGCAGT GACGTTACGA AGCGTTATAC	thal fnuDII/mvnI fnu4HI bsoFI bsoFI maeII fnu4HI bsvI lbbvI bsoFI bbvI hinPI bsaAI bsmI aluI hhal/cfoI gcattcctga cgacgaTacg cGTAAGGACT GCTGACGACG	haeIII/pali mcri eagl/xmaIII/eclXi eael cfri bsiEi ahdi/eaml105i maeIII bsmAI AGTGTCACG GCCGAGACTT ATAGTCGCTT TGTTTTTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA
ecori pfimi apoi bali 1 GAATICAACT TCTCCATACG CTTAAGTTGA AGAGGTATGA AACCTAITCC	bspMI hlnPI hhal/cfoI mstI aluI aviII/fspI hindIII 101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG CTTGACACAC GCGTCCATCT TCGAAACCTC	rsal hinPI hhal/cfol mnll cac8I haeII csp6I sfaNI 201 GGGCGTGTA CGAGGTAAAG CCCGATGCA	alui trugi pvuli msel nspBII 301 AAAGTAAT CTTTCAACA GCTGTCATAA TITTCAATTA GAAAGTTGT CGACAGTATT

```
ddeI nlaIII
                                                                                                                                                                                                                                                                                                                                                  AGCCATGGGC CCCTAGGAGA GCTCCAACTC CACTAAAATA CTTTTTCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC GATGTTTGCG
                                                                                                                                                                                                                                                                                                                                   401 TCGGTACCCG GGGATCCTCT CGAGGTTGAG GTGATTTTAT GAAAAAGAAT ATCGCATTC TTCTTGCATC TATGTTCGTT TTTCTATTG CTACAAACGC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           501 ATACGCTGAT ATCCAGATGA CCCAGTCCCC GAGCTCCCTG TCGCCTCTG TGGCCGATAG GGTCACCATC ACCTGCAGGT CAAGTCAAAG CTTAGTACAT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           TATGCGACTA TAGGTCTACT GGGTCAGGGG CTCGAGGGAC AGGCGGAGAC ACCCGCTATC CCAGTGGTAG TGGACGTCCA GTTCAGTTTC GAATCATGTA
                                                                                                                                                                                                                                                                                                                                                                      T
N
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              hindIII cap6I
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 rsal
                                                                                                                                                                                                                                                                                                                                                                                 The penultimate nucleotide was changed fr G toT ^
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               aluI
                                                                                                                                                                                                                                                                                                                                                                    F S I A
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              s
o
s
                                                                                                                                                                                                                                                                                                                                                                     M F V
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   bspMI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                sse8387I
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              E
C
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              psti
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 scfI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              bstEII hphI bsgI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             bspMI
                                                                                                                                                                                                                                                                                                                    mboli sfaNI
                                                                                                                                                                                                                                                                                                                                                                    L A S
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             V T I
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              maeIII
                                                                                                                                                                                                                                                                                                                                                                     IAFL
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              G
                                                                                                                                                                                                                                                                                                                                                                                    a mutation was found that inactivated the mluI site.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              SASV
                                                                                                                                                                                                                                                                                                                                                                     M
M
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               mplI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              acil
                                                                                                                                                                                                                                                                                                                                                                                                                                                                hgiAI/aspHI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 ec1136II
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              bsp1286
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               bsiekaI
                                                                                                                                                                                                                                                                                                                                                                                                                                                  hgiJII
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             S
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               bsrI aval aluI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              banII
                                                                                                                                                                                                                                                                                                                                                                                                                   sstI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                bmyI
                                                                                                                                                                                                                                                                                                                                                                                                                                  saci
                                                                                                                                                                                                                                                                                                      hphi
                                                                                                                                                                                                                                                                                                                   alwi[dam-] mali mali
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            tth1111/aspI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          0 S P
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               bsmFI
                                                                                                                                                                                                       mbol/ndeII[dam-]
                                                                                                                                                                                                                                       nlaIV nlaIV paeR7I kpnI cauII dpnII[dam-]
                                                                                                                                                                                         sau3AI taqI
                                                                                                                                                           xhoI
                                                                                                                                                                                                                                                                       bstYI/xhoII
                                                                                                                                                                                                                        dpnI[dam+]
                                                                                                                                                                                                                                                                                     bani bsaJi alwi[dam-]
                                                                                                                                                                                                                                                                                                      bamHI aval
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             E C
                                                                                                                                                                          mpli
                                                                             xmal/pspAI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              ecoRV
SCLFI
                                              hpaII
                              Idsm
                                                              dsav
                ncil
                                                                                                             BCLFI
                                                                                                                                                           cauli
                                                                                                                                                                          bsaJI
                                                                                                                                                                                         aval
                                                                                                                                           dsav
                                                                                                                            ncti
                                                                                             SmaI
                                                                                                                                                                                                                                                                                                    asp718
                                                                                                                                                                                                                                                                                                                     acc65I
                                                                                                                                                                                                                      csp6I
                                                                                                                                                                                                                                                                    hgici
                                                                                                                                                                                                         rsaI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           YA
                                                                                                                                                                                                                                                                                                                                                                    -23
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		•
TT & s	CCA (GT	<b>4</b> E
tfil bsmFl bpmI/gsul[dcm-] /bsp106 pleI I[dam-] hinfl GATTCTCT GGAGTCCCTT CTAAGAGA CCTCAGGGAA F S G V P S	rsal csp61 scal nl AGAGTACTCA TCTCATGAGT	acii mboli atcttcccc catctgatga gcagttgaaa tagaagggcg gtagactact cgtcaacttt
	# # C C E E E E E E E E E E E E E E E E	កំពុង ស្គឺក្នុង ស្គឺក្នុង
tfil b bpmI/gs claI/bspl06 bspDI[dam-] A TCGATTCTC T AGCTAAGAG	TACTGTTCAC ATGACAAGTG Y C S Q	CATCTGATGA GTAGACTACT S D E
t hinfi qi b clai/ bspbi caa rcg GTT AGC	r TAC	CATC
hin tagi 1 NTCCA NATCCA NATCCA NATCCA NATCCA NATCCA NATCCA	CTTA1	acii CCCGC GGGCG
tfil hinfl bsn taqI bpmI/gsul claI/bsp106 bspDI[dam-] TCCGAAACTA CTGATTTACA AAGTATCCAA TCGATTCTT AGGCTTTGAT GACTAAATGT TTCATAGGTT AGCTAAAGAGA P R L L I Y R V S N R F S	CGCAACTTAT GCGTTGAATA A T Y	acii mboli ATCTTCCGGC TAGAAGGGCG
TTACA XATGT X		
CTGATTTACA GACTAAATGT L I Y K	mboli bpual bbsI CAGAAGACTT GTCTTCTGAA	SG D D
TA CT AT GA		
SAAAC CTITG	fnu4HI bsoFI bbvI scfI pstI bsgI AGTCTGCAGC TCAGACGTCG	fnu4HI bsoFI bbvI TGGCTGCACC ACCGACGTGG
II TCCC	AGTO TCAGO	fn fn ps ps trege Acce
aluI m+j AAAGC TTTCG K A	CAGC S	[dam-]  Acre  TGC
	fnu4HI bsoFI bbvI scfI pstI pstI bsgI GACCATCAGC AGTCTGCAGC CTGGTAGTCG TCAGACGTCG	
scrF] mvaI ecoR] dsav bstN] apyI[ AAC CAC TTG GTC	rcr r	sau3AI mbol/ndell dpnl[dam+] dpnll[dam- GATC AAACG CTAG TTTGC
ACAGA FGTCT	ATTTCACTCT TAAAGTGAGA F T L	sau34 mbol/ dpn1( dpn11 GGTGGAGATC CCACCTCTAG
000	SG ATT	
bsri ACACTGGTAT TGTGACCATA B W Y	lam-] bsmFI cccTGC G T	styl bsaji rsai csp6i nlaiv , kpni hgiCi bani asp718 acc65i GCTACCAA
bsri CTACGTATTT ACACTGGTAT GATGCATAAA TGTGACCATA T Y L B W Y	1 [c]	styl bsaJ rsaI csp61 nlaIV kpnI hgiCI banI asp718 acc651 ACGTTTGGAC AGGCTACCTA T C C G G T K
ATTT TAAA L	mspl hpall bsll bsawi sau3Al mbol/adeli dpnl(dam+) dpnl(dam+) alwi(dam-) lalv stYl/xholl amHi amHi lwi(dam-) StXL/xholl stYl/xholl stYl/xholl stYl/xholl	GGAC G D
CTACGTAFFT GATGCATAAA T Y L	mspl hpail bsil bsaul saulai mbol/ndeli dpni(dam+) dpni(dam+) nlaiv bstxi/xhoil bamHi alwi(dam-) cGATCCGGT T	maeli ACGTTTGGAC TGCAAACCTG T F G Q
7.00 PA 2.00 PA 2.00 PA		
GGTATAGGTG CCATATCCAC G I G A	CTCGCTTCTC GAGCGAAGAG R P S	barbi acii bsmri TGTCCCGCTC ACAGGGGGAG
601	701	801

scrfi mvai ecoRII dsav bstNi bsaJI maeIII apyI[dcm+] GGTAACTCCC CCATTGAGG	acci cac8i AAGTCTACGC TTCAGATGCG V Y A	rmal	mael bfal sau961 haell/pall I asul rccrgcccr AGCACCGGA
mnli bsli ccrccaarcg ggaggtragc L Q S	GAGAAACACA CTCTTTGTGT E K H K	moli	madalambol/ndell[dam-] bf dpol[dam+] hgal sau961 dpol[[dam-] mspl haelll alw1[dam-] hpall sfanl asul GATCCTCTAC GCCGGACGCA TCGTGGCCTA CTAGGAGATG CGGCCTGCGT AGCACCGGGA
haell/pall hael rsal mnll csp61 cr ATCCCAGAGA GGCCAAAGTA CAGTGGAAGG SA TAGGGTCTCT CGGTTTCAT GTCACCTTCC Y P R E A R V Q W R V	fnu4HI bsoFI cellI/espI ddel bloI/bpull02I scfI mnli bbvI hgal ddel cTA CAGCTCAGC AGCACCCTGA CGCTGAGCAA AGCAGACTAC GAT GTCGGAGTCG TCGTGGGACT TCGTCTGATG Y S L S T L T L S K A D Y		aluI tru9I II aluI mseI IA AAGAGCTTCA ACAGGGGAGA GTGTTAAGCT ST TTCTCGAAGT TGTCCCTCT CACAATTCGA
haelli/pall xmnl xmnl hael rsal asp700 mnli cyb6l 17CTGGAACTG CTTCTGTTGT GTGCCTGCTG AATAACTTCT ATCCCAGAGA GGCCAAAGTA CAGTGGAAGG TGGATAACGC AGACCTTGAC GAAGACAACA CACGGACGAC TTATTGAAGA TAGGGTCTCT CCGGTTTCAT GTCACCTTCC ACCTATTGCG 132 S G T A S V V C L L N N F Y P R E A R V Q W R V D N A	maeIII 1001 AGGAGAGTGT CACAGCAG GACAGCAAGG ACAGCACCTA TCCTCTCACA GTGTCTCGTC CTGTCGTTCC TGTCGTGGAT	cac8I aluI sstI sstI sacI hgiJII hgiAI/aspHI ecl136II bstHKAI bmyI	haeIII/pall sau961 banII asu1 ddel hphl ecool091/drall maeIII alwNI[dcm-] maeIII alwNI[dcm-] ll01 CTGCGAAGTC ACCCATCAG GCCTGAGCTC GCCGTCACA GACGCTTCAG TGGGTAGTCC CGGACTCGAG GGGCAGTGT 199 C E V T H Q G L S S P V T
901 T	1001 A T		1101 C 0 199

FIG. 41D

rmal  maei  bfai hphi  xbai mnli mnli AGTCGTAAA AAGGTATCT AGAGGTTGAG GTGATTTTAT GAAAAA  AGTCGTAAA AAGGTAGA TCTCCAACTC CACTAAAATA	SCIFI	scrFI ncil mspl hpall dsav cauli bsll xmal/pspAl smal scrFI ncil dsav cauli mval bsll ecoRII
rmal maei rsai bfai csp61 spei 1201 AGTACGCAAC TAGTCGT TCATGCGTTG ATCAGCA	rsal bsiwi/spl thal funDII/mvnI bstUI bstUI bsh1236I mluI csp6I aflIII dd 1301 CTACAAACGC GTACGCT GATGTTTGCG CATGCGA	

maeli snaBl hphi bsaAl ATGTGAAAC TACGTATAAT TACCACTTTG ATGCATATTA G E T Y N	cac81 mnl1 cac81 ddel drd1 GCCTGCGTGC TGAGGACACT GCCGTCTATT CGGACGCACG ACTCCTGTGA CGCCAGATAA L R A E D T A V Y Y	sau961 haeIII/palI sau961 nlaIV hgiJII bspl286 bspl286 bspl201 bmyI	asul apal styl asul styl asul styl asul haelil/pall ecool091/drall rCGGCCTCCA CCAAGGCCC AGCCGGAGG GGTTCCGGG S A S T K G P 25chim2.fab2
bsll sau3Al mbol/ndell[dam-] dpnl[dam+] alwl[dam-] alwl[dam-] TGGATATATT GATCCTTCCA ACCTATATAT GATCTTCA	CAGATGAACA GTCTACTTGT Q M N S	maeIII bstEII scrFI	cyl dsay bsell apa.  isali dsay bsell apa.  isali bstli esp3! s.  bsayl hphl bsmBl mbll b.  rggggrchag ghacccrggr caccgrcrc rcggccrcc/Accacrcc gracercrc rcgcccrcc/Accacrcc rcgcccccc gracerc rcgcccrcc/Accacrcc rcgcccccc/Accacrcc rcgcccccc/Accacrcc rcgcaccrcc/Accacrcc rcgcaccrcc/Accacrcc rcgcccrcc/Accacrcc rcgcccrcc/Accacrcc rcgcaccrcc/Accacrcc/Accacrcc/Accacrcc/Accacrcc/Accacrcc/Accacrcc/Accacrcc/Accacrcc/Accacrcc/Accacrcc/Accacrcc/Accacrcc/Accacrcc/Accacrcc/Accacrcc/Accacrc
beaji dsav aval bstNi bsaji bsli sau961 sau961 apyi[dcm+] avali nlaIV sau961 asuI haelII/pali asuI nlaIV asuI eco01091/draII bsri eco01091/draII haelII/palI ACTGGGTCCG TCAGGCCCCG GGTAAGGGCC TGGAATGGGT TGACCCAGC AGTCCGGGC CCATTCCCGG ACCTTACCCA	thal funDII/mvnI bstUI bsh1236I bsh1236I bspMI cacttratct cgcgacaact ccaaaaacac agcatacctg GTGAAATAGA GCGTTGA GGTTTTGTG TCGTATGGAC T L S R D N S K N T A Y L		
pleI hinfI sau96I taqI xhoI paeR7I avaI maeIII bsrI e GAAGAGCTCA GTGATATGC AGTGGGTCCG TCA 29 F S S H Y M H W V R Q	thai faud haeIII/palí faud bstu sau961 sau961 nrul asuI nrul cacattca acgcccgtt cacttatct cccc ctcc ct		maell/ahinli/ahili/ahili/ahili/ahili/ahili/ahili/ahili/ahili/ahili/ahili/ahili/ahili/ahili/ahili hphi bsri mboli aatil laatil laatil laacili accerara aggaarishi accerara aggaarishi accerara aggaarishi accerara aggaarishi accerara agaarishi agaarishi abili ahili abili aatil aatili agaara agaarashi agaarashi agaarashi agaarashi agaarishi abili aatili aat

#### FIG. 41F

Ihqh	mspl hpall cfrl01/bsrFl bsaWl tthl111/aspl +) AAGGACTACT TCCCCGAACC GGTGACGGTG TTCCTGATGA AGGGCTTGC CCACTGCCAC	ddel fnu4HI mnli plei bsofi maelli mnli eco811 hinfi ddel hphi bsp1286 scfi bsu361/mst11/saul mnli bbvi bstEll bmyl bpm1/gsu1[dcm-] CCTACAGTCC TCAGGACTCT ACTCCTCAG CAGCGTGGTG ACCGTGCCT GGATGTCAG AGTCCTGAGA TGAGGAGTC GTGCCACGGA L Q S S G L Y S L S S V V T V P S	hgijii bsp1286 .ndii bmyi banii maeiii GAAAGTTGAG CCCAAATCTT GTGACAAAAC CTTTCAACTC GGGTTTAGAA CACTGTTTTG
, 96I d	fnu4HI fnu4HI bsoFI bsaJI bslI acil apyI[dcm+] bsp1286 asuI bsoFI bmyI nspBII bsaJI bbvI apyI[dcm GCGGGCACAG CGCCCTGGG CTGCCTGGTC CCCCCGTGTC GCCGGACCC GACGGACCAG G G T A A L G C L V	mspi hpali scrfi ncil dsav cauli CCCGGCTGT	taqi sali lalincII/hi bsaJi acci rCACAAGCCC AGCACACCA AGGTCGACAA AGTGTTCGCG TCGTTGTGGT TCCAGCTGTT H K P S N T K V D K
nlaIV hgiCI banI scrFI mvaI	ecoRII dsaV hgiAI/aspHI dsaV bseRI bsp1286 bpuAI apyI[dcm+] mnlI bsiHKAI bbsI bsaJI mnlI bmyI mnlI 1701 ATCGCTCTC CCCTGGCAC CCTCTCCCAA GAGCACCTCT TAGCCAGAAG GGGACCGTG GAGGAGGTT CTCGTGGAGA 129 S V P L A P S S K S T S	hinpI hhal/cfol hhal/cfol hhal/cfol hall narI hall kasI kasI hinll/acyI hgiCI haeII haeII haeII baoFI banI banI la01 TCGTGGAACT CAGGCGCCT GACCAGCGGC AGCACCTTGA GTCCGCGGGA CTGGTCGCG AGCACTTGA GTCCGCGGA CTGGTCGCG I62 S W N S G A L T S G V H T F	alui nlaIV fnu4H hgiCI bsoFI banI bbvI bsp1286 bbtXI bmyI 1901 CCAGCAGCTT GGCACCCCAG ACCTACATCT GCAACGTGAA GGTCGTCGAA CCCGTGGGTC TGGATGTAGA CGTTGCACTT 196 S S L G T Q T Y I C N V N

#### FIG. 41G

fnu4HI bsoFI haeIII/palI mcrI eagI/xmaIII/eclXI cfrI	cac81  nlaIII  nspI
fn bs hae mcri eagi/ eaei cfri	cac81  nlaIII  nspI  sspI286  sspI286  sciI aciI aciI aciI aciI  2001 TCACACATGC CCGCCGTGCC CACCACAGA ACTGCTGGG GCCGCATA  AGTGTGTACG GGCGGCACG GTCGTGGTCT TGACGACCG CCGCGTA  229 H T C P P C P A P E L L G G R M  "Junction between antibody and leucine zippen

scrFI ncil mspI hpaII	dsaV cauli	acii	Inuahi bsofi	2101 GAGAATGAAG TGGCAAGACT CAAAAAGCTT GTCGGGGAGC GCTAAGCATG CGACGGCCCT AGAGTCCCTA ACGCTCGGTT GCCGCGGGC GTTTTTAATT CTCTTACTTC ACCGTTCTGA GTTTTTCGAA CAGCCCCTCG CGATTCGTAC GCTGCCGGGA TCTCAGGGAT TGCGAGCCAA CGGCGGCCCG CAAAAAATAA	
rmaI	maeI bfaI bsmFI	sau96I pleI	haeIII/palI asuI hinfI	ACGGCCCT AGAGTCCCTA FGCCGGGA TCTCAGGGAT	
sphi ddei nlaiii celii/espi	blpI/bpu1102I hinPI nspI	hhaI/cfoI	haell nspHI, eco47III cac8I	GGGAGC GCTAAGCATG CGI CCCTCG CGATTCGTAC GCI	L V G E R O
	:		aluI	CAAAAGCTT GTCC GTTTTCGAA CAGC	K K L V
			plei	2101 GAGAATGAAG TGGCAAGACT CTCTTACTTC ACCGTTCTGA	262 ENEVARL KR

hincil/hindii alui bspDI[dam-] msei acii 2201 GTTAACTCAT GTTTGACAGC TTATCATCGA TAAGCTTTAA TGCGGTAGTT TATCACAGTT AAATTGCTAA CGCAGTCAGG CACCGTGTAT GAAATCTAAC CAATTGAGTA CAAACTGTCG AATAGTAGCT ATTCGAAATT ACGCCATCAA ATAGTGTCAA TTTAACGATT GCGTCAGTCC GTGGCACATA CTTTAGATTG

nlaIV hg1CI banI

trugi

tag1 hindIII
claI/bsp106 tru9I
bspD1[dam-] mse1 aci1

DlaIII

hpaI mseI

tru9I

aluI

msel

scrFI  wva!  mva!  ecoRII  asav  bali hpli byl[dcm+]  hinp! ban maell fok! scf!  hatcgcgrc rcgrcact rcgrcccac rccrccact raccact raccac	hhal/cfol  mael mael nhal/cfol mael nhal/cfol phel fundHI phol fun	acil fuutHI bsrl cac8l nlalV taq1 bshl236I absll alw1[dam-] hpaII acitCccccccccccccccccccccccccccccccccccc
haej sau961 scrFI ncil rsal mspl mall csp61 hpall mspl dsaV bi hpall caull cfr101/bsrFl asuI r ATGCGGTAC TGCCGGCCG	hinPI hhal/cfoI mstI bslI avill/fspI c TATGCGCACC CGT'	II[dam-] +] m-] I bslI C GACCACACC GTC
e) scfi ctgtaggcat aggcttggtt gacatccgta tccgaaccaa	foI I sfaNI ATATGCGTG ATGCAATTTC TATACGCAAC TACGTTAAA	sau3AI mbol/ndeII[dam-] dpnI[dam+] thaI fnuDII/mvnI bstUI nlaIII taqI bsh1236I ATCGACTACG CGATCATGCC GACCAC
scrFI mvai mvai ecoRII dsav nlaIV bstNI mnlI hgiCI bsaJI hhal/cfoI fokI banI maeIII fokI s TTACGCGAGT AGCACCTC GGGACCTAC GGCACCTAC GGGACCTAC GGCACCTAC GGGACTAC GGGACCTAC GGCACCTAC GCACCTAC GGCACCTAC GCACCTAC GGCACCTAC GCACCTAC GGCACCTAC GCACCTAC GGCACCTAC GCACCTAC GGCACCTAC GCACCTAC GCACCTAC GGCACCTAC GCACCTAC GCACCTAC GCACCTAC GCACCTAC GCACCTAC GCACCTAC GCACCACCTAC GCACCACCTAC GCACCTAC GCACCACCTAC GCACCTAC GCACCTACCACCACCACCACCACCACCACCACCAC	hinPI hhal/cfol rmaI maeI nheI flutHI haeII bsoFI eco47III bbvI bfaI cac8I cac8I GGGGG TGCTAGGGGT ATA	acii fnu4Hi bsoFi acii bsri cac8i nlaIV CCGCCGCCCA GTCCTGCTACT TGGAGCCACT GGCGGCGGT CAGAGCGATGA ACCTCGGTGA
nlaIV mnli hgiCI bsaJI sfol fokl banl zA TCGTCATCCT CGGCAC	maeIII sfani bsri gcar cgccagtcac targ	I BI DBII CACBI CCCA GTCCTGCTCG CTTC
hinPI hhal/cfoI 2301 AATGCGCTCA TO TTACGCGAGT A	sfi 2401 CCGACAGO GGCTĞTCG	acii fnu4BI bsoFi acii b 2501 CCGCCGCC

#### FIG. 41I

hgiJII bsp1286 bmyI	nael mspl hinli/acyl banti aau3Al cac81 real hinpl cac81 cac81 haeII haeII/bsaHl hall/bsaHl hahI/cfol cfr sfaNl cfr101/bsrFl acil cac81 hphl mboII[dam-] banII haI/cfol cfr sfaNl cfr101/bsrFl acil cac81 hphl mboII[dam-] banII nlaIII cac81 cacGCCGCC CACAGGTGCC GATGCGGCAAC ATCGCC CACATGGGC CTATATAGCC CACATCACC CACATGAGCC CACATGGCCC CACATGAGCC CACATGAGCC CACATGAGCC CACATGAGCC CACATGGCCCC CACATGGCCCC CACAGGTCCC CACATATAGCC CACATAGTGC CTACCCCCTTC TAGCCCGAGC GGTGAAGCCC CACATGCCC CACATACTCCC CACATAGTCC CACATAGTAGTCC CACATAGTCC CACATAGTAGTCC CACATAGTCC CACATAGTCC CACATAGTACTCC CACATAGTCC CACATAGTCC CACATAGTCC CACATAGTCC CACATAGTCC CACATAGTCC CACATAGTCC CACATAGTCC	BOTFI  DOIL  BOTI
hinPI hhal/cfoI lalV arI asI	hinll/acyl hgiCl haeII banI ahaII/bsaHI hphI 81 GGCG CCTATATCGC CGACATCACC	scrFI  nciI  mspI  hpaII  hpaII  caulI  haeIII/palI  haeIII/acyl  ll  lbsaJI  frI  frI  bsmFI  abaII/bsaHI  gcCCGC  gCGCCTGTTC  cCGCGTAGA  cCGCGTAGA
hinPI hhal/cfoI nlaIV narI kasI hinlI/acyI naeII	cfr101/bsrFI ban1 cac81 sgrAI haeII/pal1 hpaII eaeI hphI ahaII/bsaHI cfrI sfaNI cfr101/bsrFI acil cac8I GTGGCCGCA TCACCGCGC CACAGGTGCC GATATATCGC	scrFI  sc
msp.i	nael cfr101 cac81 haeIII/ eael ' cfr1 81 2601 GTGGCCGCC	2701 CTTGTTTC

#### FIG. 41

mbli bali bari bbvi bali hibfi hibfi hgai sfaNi bali alui bali 2801 CCTCAACCTA CTACGGCT GCTCCTAAT GCAGGAGTCG CATAAGGGAG AGCGTCGTCC GATGCCCTTG AGAGCCTTCA ACCCAGTCAG CTCCTTCGG GCAGTTGGAT GATGACCCGA CGAAGGATTA CGTCCTCAGC GTATTCCCTC TCGCAGCAGG CTACGGGAAC TCTCGGAAGT TGGGTCAGTC GAGGAAGGCC

plei

ecoNI bali

bsofi bsri bbvi

fpu4BI

mspI hpaII bsaWI

bsrI aluI bslI

fnu4HI  mspI hinPI  naeI haeII  cfr101/bsrFI  cac81 eco47III  bpuAI  bbsI hgiCI bbvI  bbsI hai/cfoI mnlI  cttatGACTG TCTTCTTTAT CATGCAACTC GTAGGACAGG GCTCTGGGTC ATTTTCGCG  GAATACTGAC AGAAGAATA GTACGTTGAG CATCCTGTCC ACGCCGTCG TAAAAGCCGC	sau961 nlaIV avaII acil tfiI cac8I mnlI maeIII bsmFI GCTTGCGGTA TTCGGAATCT TGCACGCCCT CGCTCAAGCC TTCGTCATG GTCCCGCCAC CGAACGCCAT AAGCCTTAGA ACGTGCGGA GCGAGTTCGG AAGCAGTGAC CAGGGCGGTG	mcrI eagl/xmalli/eclXi eael hinPl cfrI hhal/cfol thal mspl bsiEl thal nael fnu4HI fnuDII/mvnI fnuDII/mvnI cfr101/bsrFI bstUI bstUI bstUI cac8I acii hgal bsh1336I hael bglI nlalII haelII/palI maelI cac8I nruI bsh1236I fokI haelI cGCGGCATG GCGCCGACG CGCTGGCTG GATGGCCTTC GCGCCGTAC CGCCGCACG CGCACGCTC GCGCCGTAC CGCTCGCACG CGCACGCACG GCGCCGTAC CGCTCGCACG CGCTCGCACG CGCCGCACG CGCTCGCACG CGCCGCACG CGCTCGCACG CGCCGCACG CGCTCGCACG CGCCGCACG CGCCGCACG CGCCGCACG CGCCGCACG CGCCGCACG CGCCGCACG CGCCGCACG CGCCGCACG CGCCCGACC CGCCGCACG CGCCCGACG CGCCCGACG CGCCCGACG CGCCCGACG CGCCCGACG CCCCGCACG CCCCGCACG CCCCGCACG CCCCGCACC CCCCGCACC CCCCGCACC CCCCGCACC CCCCGCACC CCCCGCACC CCCCGCACC CCCCCCCACC CCCCCCCACC CCCCCCCACC CCCCCC
mboli bpual bbsi nlaili CTTATGACTG TCTTTTAT CATGCAACTC GTA	nli acii tfii cac81 hinfi GCTTGCGGTA TTCGGAATCT CGAACGCCAT AAGCCTTAGA	
acil thai thai fuuDII/mvni bstJi nlaIII acil hinpi bcgi fuu4HI hhai/cfoI bsoFi 2901 TGGGGGGG GCATGACTAT GGTCGCGCGA ACCCGCGCC CGTACTGATA GCAGGGGGT	thal fnuDII/mvnI bstUI bstUI sau961 avalI avalI asuI bpmI/gsu1[dcm-] bpmI/gsu1[dcm-] acgaccccrr rccrccccccccccccccccccccccccc	mspi naeli cfrl01 haelil/pali hpali psp1406i cac8i bgl1 n 3101 CAAACGTTC GGCGAGAAGC AGGCCATTAT CGCCGGC

#### FIG. 41K

- Даш- ]		
alui alwi[dam- PAGCTTCAAG	nlaiii GGTTGGCATG CCAACCGTAC	fnu4HI bsoFI acil II nlaIV hgiCI 01/bsrFI II banI G CGGCACCTCG
bsmFI aluI a. CCATCAGGGA CAGCTTCAAG	./aspHI 186 AI nlaIII ACATGGAACG	msp hpa naei cfri cac8 TGGAAGCCG
bspMI scrFI mvaI ecoRII dsaV bstNI apyI[dcm+] AGGTCCGTCC ATCTACTGCT	aJI aJI ca crcesc	haeIII/palI au96I FI I I II N sul taql II mnli GGCCACC TCGACCTGA
bspMI scrFI mvaI ecoRII dsaV pall bstNI [II apyI[dcm+] scrG rccAGGCAGG	m lam-] acil fnu4H bsoFI bglI 3CGA TTTATGCCGC	haeII sau96I scrFI nciI mspI hpaII dsaV nlaIV asuI III cauII GGAG CCGGCCA
bspMI thal scrFI fnuDII/mvnI mvaI bstUI ecoRII bstUI dsaV bsh1236I haeIII/pall bstNI acil cac8I nlaIII apyI[dcm+] ccGCGTTGCA GGCCATGCTG TCCAGGCAGG TAGATGACGA CCATCAGGGA CAGCTTCAAGGGGACGT CCGGTACGACGT AGGTCCCTC GTCGAAGTTC	4HI  I sau96I avali  Avali asula mbol/ndell[dam-] bsuli hgiAl  Sau3AI asul mbol/ndell[dam-] bspl1  acil bspl1  acil dpn1[dam-] dpn1[dam+] bsoFI bmyl  taq1[dam-] acil dpn1[dam+] bgl1 cac8I  CGGAGAATGC AGCCTAACTT CGATCACTGG ACCGCTGAC  CCGAGAATGG TCGGATTGAACTT GGACTGC CTGGCGCACC  CGGAGAATGG TCGGATTGAACTT GGACTGC CTGGCGCTCG	thai fnuDii/mwni bstUi bshl236i acii nla acii nla
thai fnuDI bstUI cac81 I sfaNI bsh12 I fokI aciI TCGGGATGC CCGCGT	sau961 avall ss. sau3Al asul ml mbol/ndell[dam-] dpnl[dam+] nspBll dpnl[dam-] acil dl tcql[dam-] acil dl T CGATCACTGG ACCGCTG	thal fnuDII/mvnI bstUI bsh1236I mnlI aciI hgaI CCTCCCGGG TTGCGT
fnu4HI bsoFI acil mspl msll sfaNI hpaII sfaNI TTCCGGCGGC ATCGGGATGC	sau ava bsrI sau3AI asu mbol/ndeII dpnI[dam+] taq1[dam-] taq1[dam-]	
fnu4HI bsoFI acil acil cac tfiI mspI mslI sfaNI hinfI hpaII sfaNI fokI 3201 CCCATTATGA TTCTTCTCGC TTCCGGCGGC ATCGGGATGC GGGTAATACT AAGAAGAGCG AAGGCCGCG TAGCCCTACG		fnu4HI bsoFI hinPI hhal/cfoI nlaIV narI kasI hinll/acyI hgiCI haeII banI aciI ahaII/DsaHI CTAACATCG GGGGGGATA TGGAACAGAC
3201 CCCAT1	fnu bso aci thal fnuD bstU cac8I sau3AI bshl mboI/ndeII[ dpnI[[dam-] dpnI[[dam-] 3301 GATCGCTCGC CTAGCGAGCG	3401 GATIG

#### FIG. 41L

hgal thal acil fnuDII/mvbI bstUI bsh12361 ATCCA TCGCGTCCGC				Idsu	H		ncil	dsav	sau96I		cac8I	rmaI	mael	/dra	bfal acil	ACCCG GCTAGGCTGG	TGGGC CGATCCGACC
styI bsaJI CCTTGGCAG AACAT					hpall	SCLFI				nlaIV	avall	asuI	IMndd		mnli cauli-bfal	CTGTCGT TGAGG	GACAGCA ACTCC
hinPI hhal/cfol mstI pflMI avill/fspI st i bslI bs ic cGCAAACCAA CCC	-							sau3AI	mbol/ndeII[dam-]	dpnI[dam+]	hinPI dpnII[dam-]	hhal/cfol hgiAl/aspHI	mstI nlaIII bsp1286	avill/fspl bsiHKAI	DmyI	G CATGATCGTG CTC	C GTACTAGCAC GA(
h h ms av I GAGA ACTGTGAATG	haeIII/palI mscI/balI	haeI	SCIFI	mval dsal	ecoRII	dsaV	bstNI	bslI bsaJI	apyI[dcm+]			asul eael hhal/cfo	E	cfrI	eco01091/drall msll	reec cacegerec	SACCG GIGCCCACG
acil ATCAATT CTTGCGG IAGTTAA GAACGCC			98	'n	9	ds	sq	sq	ap	196nes	avall	asuI	fnu4HI ppuMI		bbvI eco010	CAGCGIT GGGIC	GICGCAA CCCAGO
hhal/cfol hhal/cfol hhal/cfol mstl pflMI fouDII/mv  tfil pflMI aviII/fspl styl hinfl bsll bsaJI bsaJI bshl236I  CTAACGGATT CACCACTCCA AGAATTGAG CCAATCAATT CTTGCGGAG ACTGTGAATG CGCAAACCAA CCCTTGGCAG AACACTAAA GACGCTTAA GACGCTTA								fpu4BI	thal hinPI	fnu4HI bsoFI	bsoFI fnuDII/mvnI	batul	hal/cfol		bomI/gsul[dcm-] acil sfaNI b	CACGC GGCGCATCTC GGG	gtagaggice tegecetece eegegtagag eeegtegeaa eeeaggaeeg gtgeeeacge gtactageae gaggaeagea aeteetggge egateegaee
hinp!  hal/cfol  hal/cfol  hal/cfol  mstl pflMI  tfil pflMI  avill/fspl styl  bstUl  hinfl bsull  craccatcca agaattggag ccaatcaatt cttgcggaga actstagatg cgcaaaccaa ccttggcag aacataagg agcgtccgc  gattgcctaa gtggtgaggt tcttaacctc ggttagttaa gaacgctct tgacacttac gcgttggtt ggcaaccac ttgtataagg agcgaaggg		,								fout	Posd	fnu4HI	C TECAC	bbvI act	bomI/qsuI (dcm	3601 CATCTCCAGC AGCCGCACGC GGCGCATCTC GGGCAGCGTT GGGTCCTGGC CACGGGTGCG CATGATCGTG CTCCTGTCGT TGAGGACCCG GCTAGGCTGG	GIAGAGGICG ICGGC

#### FIG. 41M

fnu4HI bsoFI bbvI

fnu4HI

fauDII/mvaI

bstul

hphI tfiI

cac8I

thaI

bsoFI

sau3AI

am-]	fnu4BI bsoFI bbvI sfaNI fokI cacBI scaGGATGCT GGTCCTACG	bari mnli
mbol/ndeIl[dam-] mamI[dam-] dpnI[dam+] dpnII[dam-] bstYl/xhoII alwI[dam-]	mspI hpaII mrol bsaBI[dam-] bspMII bspEI[dam-] bsaWI sfaNI accIII[dam-] TTATGTTCCG GATCTGCATC G	acil boki sau96i sfani nlarv acil avali fnu481
	acil thai fnuDII/mvnI hinPI bstUI hhaI/cfoI bshl236I haeII mslI GGAAACGCG GAAGTCACCG CCCTGCACCA	cac81 hinPI hhal/cfoI haelI eco47111
	mspl hpall thal thal thal bppMII bppMII bpuAI  bpuAI  bpuAI  bpuAI  bpuAI  bpuAI  bpuAI  bpuAI  bpuAI  bpuI  bpuI  bpuI  bpuI  bpuI  bpuI  bpuI  bpuI  cacli   dam-   fout accli cacli  cacli ca	hin haha tru91 hae11 mse1 eco47

3901 CIGIGGAACA CCTACAICIG TAITAACGAA GCGCIGGCAI IGACCCIGAG IGAITITICI CIGGICCCGC CGCAICCAIA CCGCCAGIIG IITACCCICA GACCCCIAGI GGCGGICAAC AAAIGGGAGI GACACCIIGI GGAIGIAGA AIAAITGCIAA AAAIGGGAGI

Idsu

SCLFI nctI Idem 4001 CAACGTTCCA GTAACCGGGC ATGTTCATCA TCAGTAACCC GTATCGTGAG CATCCTCTT CGTTTCATCG GTATCATTAC CCCCATGAAC AGAAATTCCC GTTGCAAGGT CATTGGCCCG TACAAGTAGT AGTCATTGG CATAGCACTC GTAGGAGAGA GCAAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGGG

ball

apol

nlaIII

mplI fokI sfani

maeIII

maelli nspHI

psp14061 maell

cauli hpall

dsav nlaIII

ball berI

				<pre>pbmI/gsuI[dcm-]</pre>	CGCIICIGGA GAAACICAAC	GCGAAGACCT CTTTGAGTTG
			tru9I	mseI	CAGACATTAA	GTCTGTAATT
cac8I	sau96I	tru9I haeIII/pali	msel asul	acil bsli nlalii acil	4101 CCTTACACCA AGGCATCAAG TGACCAAACA GGAAAAAACC GCCCTTAACA TGGCCCGCTT TATCAGAAGC CAGACATTAA CGCTTCTGGA GAAACTCAAC	GGAATGTGCC TCCGTAGTTC ACTGGTTTGT CCTTTTTTGG CGGGAATTGT ACCGGGCGAA ATAGTCTTCG GTCTGTAATT GCGAAGACCT CTTTGAGTTG
			BfaNI	mpli maelil	4101 CCTTACACG AGGCATCAAG TGACCAAACA	GGAATGIGCC ICCGIAGIIC ACTGGITIGI
			_			

									hphI	201 GAGGTGGAG CGGATGAACA GGCAGACATC TGTGAATCGC TTCACGACCA CGCTGATGAG CTTTACCGCA GCTGCCTCGC GCGTTTCGGT GATGACGGTG	CHICARCTIC GCTACTIGE COGICTICAGE ACACTIDAGG AAGIGCIGGI GCGACTIC GAAAIGGCGI CGACGGAGCG CGCAAAGCCA CIACTGCCAC
	Idai			<b>—</b>		Id		H	hphī	rcccr o	AGCCA
CITAL	fnuDII/mvnI	bstul	hinpi	nhaI/cfoI	н	fauDII/mvnI	П	mnli bsh1236I	acil bbvi bsh12361 hphI	GCGTT	CGCAA
		Ω	ų	됲	thaI	fon	bstul	mnli b	psh	CCTCGC	GGAGCG
TUANIT	bsoFI	aluI	pvuII	nspBII	fou4HI	bsoFI		ppvI	PPVI	A GCTG	T CGAC
		•	Ď,	ā	fo	pa	bcgI	qq	acil	TACCGC	ATGGCG
									alul	AG CTT	TC GAA
						•	٠			SCTGATG	CACTAC
									mslI	ACCA CC	rggr g
										rTCACG!	AAGTGC
						XmbI	tfil	hinfi	asp700	TGAATCGC	ACTTAGCG
										CATC TG	GIAG AC
								·		GGCAGA	CCGTCT
						fnuDII/mvnI		1961	oki	GATGAACA	CTACTTGT
				acil	thal	fauDI	batul	bah1236I	alul haal foki	ACG CG	
									Alul b	CACCTGG	
										102	1

	hgal thal fauDII/mvnI	bsh12361 hinPI nspBII hhal/cfoI	CGGTCACAGC TIGICIGIAA GCGGAIGCCG GGAGCAGACA AGCCCGTCAG GGCGCGTCAG CGGGTGITGG GCCAGIGICG AACAGACAII CGCCIACGGC CCICGICIGI ICGGGCAGIC CCGCGCAGIC GCCCACAACC
1 *	scrFI ncil mspl	sfaNI foki dsaV acii cauli drdi	TCTGTAA GCGGATGCCG GGAGCAGACA AGACATT CGCCTACGGC CCTCGTCTGT
esp3I bsmBI bsmAI		DDVI DCII DAIII dsaV DSPI Cauli alui DSPHI Alui bsli maelli	G ACACATGCAG CTCCCGGAGA

#### FIG. 410

hgiAl/aspHI bsp1286 bsiHKAI bmyl ndel apaLl/snol alw441/snol GTGCACC	TCG AGC	/pali CAA GTT	ວອຸ
AGA	foI mcrI bsiEI cGGTCGTTCG	bsli cac@l haeIII/palI haeI AGGCCAGCAA TCCGGTCGTT	mnll CAGAGGTGGC
ddeI rsaI csp6I GATTGTACTG CTAACATGAC	hinPI hhal/c fnu4HI bsofI I bbvI rcgcTcccr	nlaiii nspi nspui afliii GGAAAGACA TGTGAGCAAA	vbl  tell  acil  blaIV  creccettt tccatagect ccecccct gacgagcatc acaaaaatcg acettcaagt cagagcacccg gacgagcatc acaaaaaatcg acettcaagt cagagcacccg gacacaaaa aggaatcaa gecgagaga ctgctcgtag tettttagc tgcgagttca gtctccaccc
sfani 4Hi Fi G CATCAGAGCA			hgi dri taqi ACAAAAATCG
fnu bso aci ACTATGCG	mboll earl/ksp6321 sapl hinPl hhal/cfol haell acil mnll AGGCGCTCTT TCCGCGAGAA GGCGAAGGAG	GGATAACGCA	sfani GACGAGCATC
bst11071 tru9] accl bsri msel GT ATACTGGCTT A	mboli earl/k sapi hinpi hhal/cfol haeli AGGCGCTCTT	tfil hinfi CAGAATCAGG	acil nlaIV TCCATAGGCT CCGCCCCT AGGTATCCGA GGCGGGGGA
	sfani acii ATACCGCATC TATGGCGTAG	CGGTTATCCA	nlaIV nccatagect or Aggrateds
maeli III saal spi ACGTAGCGAT	TAAGGAGAAA	acil GGCGGTAATA CCGCCATTAT	E 67 H
fnu4HI bsoFI bbvI hinPI nlaIII bsrI bsaAI hhal/cfoI tth1111/aspI 4401 CGGGTGTCGG GGCGCAGCCA TGACCCAGTC ACG	acil sfaNI 4501 ATATGCGGTG TGAAATACCG CACAGATGCG TATACGCCAC ACTTTATGGC GTGTCTACGC	fnu4HI bsoFI acil fnu4HI acil bsoFI bsrBI bbvI cac8I aluI cCGCGCGC CCCCATAGTC GAGTGAGTTT	fnuDII tUI h1236I acii fnu4HI bsoFI haeIII/pa
fnu4HI bsoFI bbvI hinPI nla hhaI/cfoI GGGGCAGCCA	acii TGAAATACCG (	acil bsrBi alui GA GCGTATCAG C	scrFI the mval ecoRII bst dsay bst bstNI bslI apyl[dcm+] haeII/palI haeI nlalv AAGGCCAGGA ACCGTAAAAA TTCCGGTCT TGGCATTTT
CGGGTGTCGG	acii ATATGCGGTG	fnu4HI bsoFI acii fnu4HI bsoFI bsr bbvI cac8I GCTGCGCCGA	scrFI the myal myal ecoRII bs dsav bs! bs! bstNI bs!I apy1[dcm+] haeIII/pal! haeI nlalv trccGGTCGT TGGCATTTT
4401	4501	4601	4701

#### FIG. 41P

acil mspl fnu4HI hpall bsofi bsaWI acil GACCCTGCCG CTTACCGGAT ACCTGTCCGC	hgial/aspHI bsp1286 bsiHKAI bmyI bmyI apaLI/snoI aluI alw441/snoI caaccaca accccac accccaca accccaca accccaca	alwNI[dcm-] fnu4HI bsoFI bsoFI bbvI bsrI bsvI bsrI bsvI cc ACTGGCAGCA GCCACTGGTA	maei bfai cactagaagg acagtatttg gtatctgggg gtgatcttcc tgtcataaac catagacgcg
bsli bsssi I muli hhal/cfoi rcc crcstsccr crcrstrcc	scfi cgctgtaggt atctcagttc ggtgtaggtc gttcgctcca gcgacatcca tagagtcaag ccacatccag caagcgaggt	mspi hpali scrfi ssawi plei dsav hpali tauli rccgtaact atcstcttga GTCCAACCC GTAAGACACG ACTTATCGCC	beli mai mael scfi haelil/pali mael haeli hael bfai bfai stgctacaga gttcttgaag tggtgccta actacggcta cactagaagg cacgatgtct cagaacttc accaccgat tgatgccgat gtgatcttcc
SCIFI  SCIFI  SCIFI  MASI  CCORII  CCO	hinPI hhal/cfol haeli alul so 4901 CTTTCTCCCT TCGGGAAGCG TGCCGTTTC TCATAGCTCA CGCT GAAAGAGGA AGCCTTCGC ACCGGAAAG AGTATCGAGT GCGA	fnu4HI bsoFI nspBII acii hinPI mspI mcri bbvI bsiEI hhal/cfoI hpaII 5001 CCCCCGTTC AGCCCGACC CTGCGCCTTA TCCGTAACT ATCC	mnli acii sefi 5101 acaggattag cagagcgagg tatgtaggcg gtgctacaga gttc tgtcctaatc gtctcgctcc atacatccgc cacgatgtct caag

FIG. 41Q

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fnu4HI bsoFI bbvI cac8I TT TTTTGTTG CAAGCAGCAG	tru9I nlaIII mseI rcaI maeII bspBI TC ACGTTAAGGG ATTTTGGTCA AG TGCAATTCC TAAAACCAGT	TAAACTTGGT ATTTGAACCA AGATAACTAC	
acii T AGCGGTGGTT A TCGCCACCAA	A ACGAAAACTC T TGCTTTGAG	ral CAATCTAAAG TATATATGAG GTTAGATTTC ATATATACTC pleI hinfi ahdi/eaml1051	G GGGCAGCACA
<pre>tI[dam-] +) n-] acii saaacaaac CACCGCTGGT GTTTG GTGGCGACCA</pre>	hgal ddel GGGTCTGAC GCTCAGTGGA ACGAAAACTC	tru91 mse1 ahaIII/dra1 AGTTTAAAT CAATCTAAAG TATATATGAG TCAAAATTTA GTTAGATTTC ATATATACTC ple1 hinf1 fok1 ahd1/eam11051 carccatagt tGCCTGACTC CCGTGTT	
mspI hpaII sau3AI mboI/ndeII[dam-] dpnI[dam+] dpnII[dam-] aluI alwI[dam-] TCAACCATCG AGAACTAGG CGTTTGTTG	sau3AI 3AI mbol/ndeII{dam I/ndeII[dam-] am-] dpnI[dam+] dpnII[dam-] II[dam-] I(dam-] /xhoII CCTTTGA TCTTTTCTAC GGAAACT AGAAAAGATG	tru9I msel drai TTAAAAATGA AATTTTTACT AATTTTTACT iI[dam-] i+] crarttCGTT	
maeIII bsri ccagttacct tcggaaaag AG	sau3AI mboI mboI/ndeII[da dpnI[dam+] dpnII[dam-] bstYI/xhoII alwI[dam-] bs AAAAGG ATCTCAAGAA		CCAATGCTTA ATCAGTGAGG CACCTAICIC A GGTTACGAAT TAGTCACTCC GTGGATAGAG T
eco571 b 5201 TCTGCTGAAG C AGACGACTTC G	hinpi hhai/cfoi thai fnuDii/mvni bshliji 5301 ATTACGCGCA GAAA TAATGCGCGT CTTT	5401 TGAGATTATC A ACTCTAATAG T Eru9I	5501 CCAATGCTTA A GGTTACGAAT T

haeIII/pall sau961 hinPl asul AGGGCGAGC	scrFI ncil mspI hpall rmal hpall rmal hpall cauld avall avall asel/asnl/vspI alul scrcccaact ttatcccct ccatcact tattattataca accented at accented accelerated accented accente	cac8I scfi scfi psti psti psti fbu48I bsoFI bbvI msli bstDl bsgI sfaNI maeIII bstCCATGCCATC TCGCGCACCACG TTCGTATGG CTTCATTCAG GCCCAAGG GTTGCTAGTT CGCTCAATG TACTAGGGGG ACAACGGTAA CGACGTCAAG TACTAGGACAAC TACTAGGGGG ACAACGGTAA CGACGTCAAG AACCATACC GAAGTAAGTC GAGGCCAAGG GTTGCTAATG TACTAGGGGG
bsal bsal bsal bsal bsal thal thal sau96	scrfi ncii mspi hpali rmal hpali mael avali msel cauli bfal bsrl msel saul 5701 GCAGAAGTGG TCCTGCAACT TTATCCGCCT CCATCCAGTC TATTAATTGT TGCCGGGAAG CTAGATCGCT CATTATAATAACT CGTCTTCACC AGGACGTTGA AATAGGCGGA GGTAGGTCAA ACGCCCTTC GATCTCATTC ATCAATACAA	sau3AI mbol/ndeII[dam-] dpnI[dam+] maeII GATCAA GGCGAGTTAC
CAATAAACCA	bsz TAGTTCGCCA	sau3AI mboI/ndeII dpnI[dam+] c CAACGATCAA GGC G GTTGCTAGIT CCG
bpm1/gsu1[dcm-] :I 1/bsrF1 :aIV :CTCCA GATTTATCAG	rmal mael bfal alul AG CTAGAGTAA(	nlaIV mspI bsaWI aluI hpaII .AG CTCCGGTTC
bpm1/gs' msp1 hpa11 cfr101/bsrF1 hph1 nla1V TC ACCGCTCCA G	scrfi ncii mspi hpaii dsav cauii L/vspi a	a CTTCATTCA CC GAAGTAAGT
bsmAi bsal thai fuuDil/mvni bstUi bsh1236i hcii cccGAG ACCCACGCT	scri nci: msp: hpa: tru9I dsa! aseI/asnI/vspI c TATTAATTGT TGCCG	CG TTTGGTAT
bsmAI bsaI thaI fnuDII/m bstUI bsh1236I aciI G ATACCGCGAG A	mpli bsri I foki sccr ccarccagi	telli tc accetectics
bsrl fnu4HI nlary bsoFI haeIII/pall bsrDI asul bbvI GGCCCCAG TGCTGCAAT	mD acii I TTATCCGCC	mali fani ca TcGTGGTGT
bsrl sau961 nlaIV haeIII/po asuI r CTGGCCCAG	sau961 avali asul GG TCCTGCAAC	caceli scfi psti fnu4Hi bsoFi bbvi m Di bsgi sf T GCTGCAGGC
1 GGCTTACCAT	8 a. a. 1 GCAGAAGTG	ber 1 TGTTGCCAT ACAACGGTA
560.	570	580

# acii alui asui bsiEi 5901 ATGTTGTGCA AAAAAGCGGT TAGCTCCTTC GGTCCTCCGA TCGTTGTCAG AAGTAAGTTG GCCGCAGTGT TATCACTCAT GGTTATGGCA GCACTGCATA TACAACACGT TTTTTCGCCA ATCGAGGAAG CCAGGAGGCT AGCAACAGTC TTCATTCAAC CGGCGTCACA ATAGTGAGTA CCAATACCGT CGTGACGTAT

fou4HI bsofI bbvI

nlaIII

haeIII/palI acii fnu4Hi bsoFi

mnll dpni[[dam-] sau961 pvul/bspCI

gau3AI
mbo1/ndeII[dam-]

dpnI[dam+]

eael

_	sau3AI mbol/ndeII[dam- dpnI[dam-] dpnII[dam-] stYl/xhoII lwI[dam-] GATC	
CGAGTTGCTC GCTCAACGAG	sau3AI mbol/ndeII dpn![dam+] dpn!I[dam+] bstYl/xhoII alw![dam-] CTCAAGGATC GAGTTCCTAG	
fnu4HI bsoFI aciI ATGCGGCGAC TACGCCGCTG	GGCGAAACT	
ddel AGTCATTCTG AGAATAGTGT TCAGTAAGAC TCTTATCACA	hei psp1406i xmni asp700 mboli CATTGGAAAA CGTTCTTCGG	
rsal scal I csp61 GAG TACTCAACCA	hgial/aspHI bsp1286 tru9I bsiHKAI mseI bmyI ahaIII/draI TTTAA AAGTGCTCAT CA	eco57I
rsal bsri scal NI maelli hphi csp6i GCTTTTCTGT GACTGGTGAG TAC	hinPI hhal/cfol thal fuuDII/mvnI bstUI bshl236I clI cGC GCCACATAGC AGAACTTTAA GCG CGGTGTATCG TCTTGAAATT	hgiAI/aspHI bsp1286
:I sfaNI TCCGTAAGAT G AGGCATTCTA C	hinPl hhal, thal fhuDll bstUI bshlZ: acil acil ATAATACCGC GC	tagī
foki bsrl scal ddel bsofi scal ddel acti acti scal ddel acti scal brotenseri by booki acti acti articroterecea tecesare acticroterecea tecesare acticroterecea tecesare acticroterecea tecesare acticroterecea tecesare acticroterecea tecesare acticroterecea tecesare actica arcecea tecesare actica arcecea tecesare actica arcecea actica acti	hgai hinli/acyl hinli/acyl hall/cfol mspl mspl hal/cfol h	bsrI sau3AI
9	61	

 $\overline{1}$ 

bsiEI bcgI

mcrI

6301 GAAGGCAAAA TGCCGCAAAA AAGGGAATAA GGGCGACACG GAAATGTTGA ATACTCATAC TCTTCCTTTT TCAATATTAT TGAAGCATTT ATCAGGGTTA CTTCCGTTTT ACGGCGTTTT TTCCCTTATT CCCGCTGTGC CTTTACAACT TATGAGTATG AGAAGGAAAA AGTTATAATA ACTTCGTAAA TAGTCCCAAT

sspI

ear1/ksp6321 Ilodn

mslI

fau4BI acti

6201 TTACCGCTGT TGAGATCCAG TTCGATGTAA CCCACTCGTG CACCCAACTG ATCTTCAGCA TCTTTTACTT TCACCAGCGT TTCTGGGTGA GCAAAAACAG AATGGCGACA ACTCTAGGTC AAGCTACATT GGGTGAGCAC GTGGGTTGAC TAGAAGTCGT AGAAAATGAA AGTGGTCGCA AAGACCCACT CGTTTTTGTC

dpnII[dam-] dpnI[dam+]

alw44I/snoI apaLI/snol

bssSI

maelil

bstYI/xhoII

alwI[dam-]

nspBII

**DSIHKAI** bmyI

mpol/ndeII[dam-]

dpnII[dam-]

dpnI[dam+]

hphI

mbol/ndeIl[dam-] sau3AI sfaNI mboII[dam-]

bemai berbi bemai berbi 6401 tigicicatg agcggataca tattigaatg tattiagaaa aataaacaaa taggggticc gcgcacatti ccccgaaaag igccacctga cgictaagaa Aacagagtac icgcctaigt ataaacttac ataaaictti tiattigiti aiccccaagg cgcgigtaaa ggggcititc acggiggaci gcagaiicti ahali/bsaHi aatii ddei hinli/acyi maell fauDII/mvnI bstUI bsh1236I acil thaI bpuAI bbsI eccol091/drall haeIII/pali asuI sau96I mplI basSI tru9I mseI plaIII Dapel rcal bspHI acil DlaII rcal

hinPI

#### FIG. 410

6501 ACCATTATTA TCATGACAIT AACCIATAAA AATAGGGGGIA TCACGAGGCC CITTCGTCTT CAA TGGTAATAAT AGTACTGTAA TTGGATATTT TTATCCGCAI AGTGCTCCGG GAAAGCAGAA GTT

```
2628 2781 2784 2787 2906 2926 3005 3045 3094 3141 3226 3241 3309 3342 3367 3412 3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266 4351 4390 4400 4442 4467 4505 4518 4544 4561 4604 4611 4632 4723 4751 4878 4897 5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
                                                                                                                                                                                                                                                                                                                                                                     ahdı/eamılosı(GACNNNNGTC): 346 5566
72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2126
aluı(AGCT):
2218 2233 2889 3292 4202 4259 4210 4319 4338 4619 4845 4935 4981 5238 5759 5859
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463
                                                                                                                         178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         640 999 1347 1357 1449 1665 1713 1755 1764 2333 3262 3645 4705 4826 4839
                                                                                                                                                                                                                                                                                                                           1645 1813 2616 2637 2751 3408 6107 6489
                                                                                                                                                                                                                                                                                                                                                                                                                                                                             1831 4494 4992 6238
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      1831 4494 4992 6238
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            905 930 4234 6166
                                                                                                                                                                                                                                                                                                                                                       5435 5454 6146
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     1117 1385 5089
                                                                                           1093 1963 4449
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  see tthilli
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                                                                                                                  3867[dam-]
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                                                                                                                                                                                                                                                                                     1307 4678
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                see hgiAI
                                           1645 6489
                                                                                                                                                                                                                                                              see hinli
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       see asel
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      403 823
                                                                    403 823
                                                                                                                                                                                                                                                                                                             1788
                                                                                                                                                                                                                                                                                                                                                                                                                                                           5922
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                5742
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            alwni [dcm-](CAGNNNCTG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                asel/asnl/vspl(ATTAAT):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    alw44I/snoI(GTGCAC):
                                                                                                                                                                                                                                                                                                                                         ahall/bsaEl(GRCGYC):
                                                                                                                                                                                                                                                                                                                                                              ahaiii/drai(TTTAAA):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           apaLI/snoI(GTGCAC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               asp700 (GAANNNTTC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           alwI[dam-](GGATC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       apy1[dcm+](CCWGG):
                                                                      acc651 (GGTACC):
                                                                                                                     accili(TCCGGA):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           asp718(GGTACC):
                                                                                                                                                                                                                                                                                        aflii(ACRYGT):
                                             aatii(GACGTC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    apol(RAATTY):
                                                                                             accI(GTMKAC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   apal(GGGCCC):
>length: 6563
                                                                                                                                                                                                                                                                                                                   ageI(ACCGGT):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   agul (GGNCC):
                                                                                                                                          acil(CCGC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    aspHI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 asuI
```

FIG. 41V

Stop-Template Primer

5' CAT GGT ATA GGT TAA ACT TAT TTA CAC 3' SL.97.2

5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3' NNS Randomization Primer SL.97.3

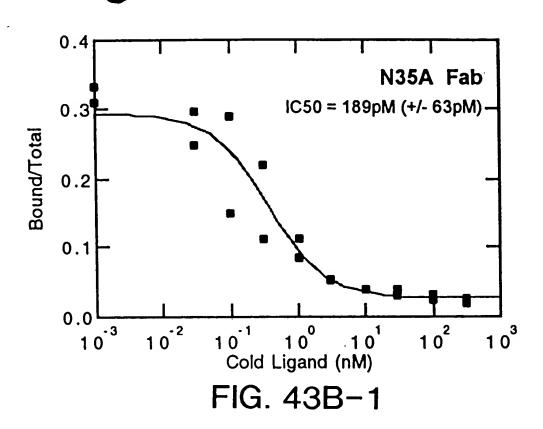
FIG. 42

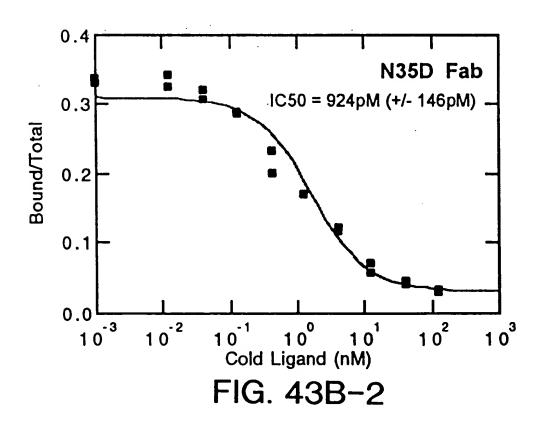
Randomization of Position N35 of Variable Light Chain CDR-1 Amino Acid Frequency

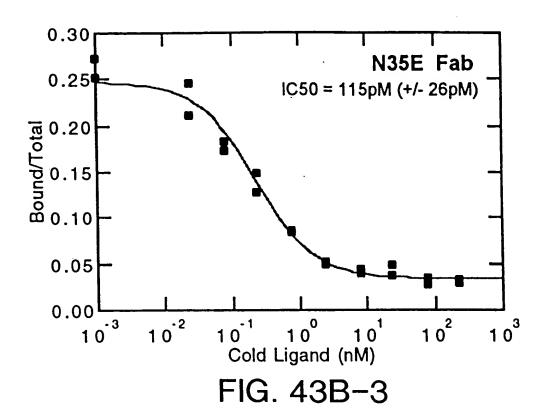
Phage Display (NNS Codon Library) Sort #3

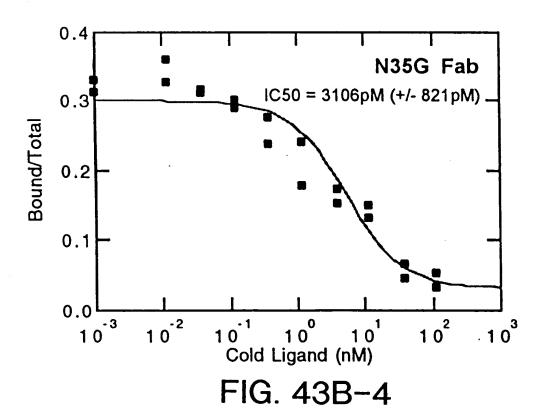
Frequency % Total
22.2
5.6

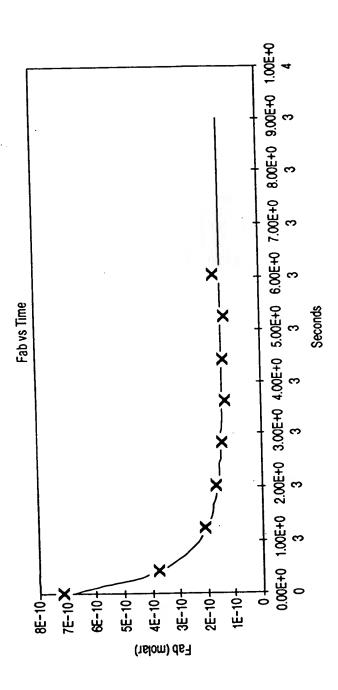
FIG. 43A











Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.F(ab')2.

CAMPLE	K B	kd	Na
6G4V11N35A-Fab	R	<u>R</u>	114pM
6G4V11N35A-F(ab') <sub>2</sub>	2.0×10 <sup>6</sup>	2.1x10 <sup>-4</sup>	109pM
6G4V11N35E-Fab	4.7×10 <sup>6</sup>	2.6x10 <sup>-4</sup>	54pM

FIG. 44

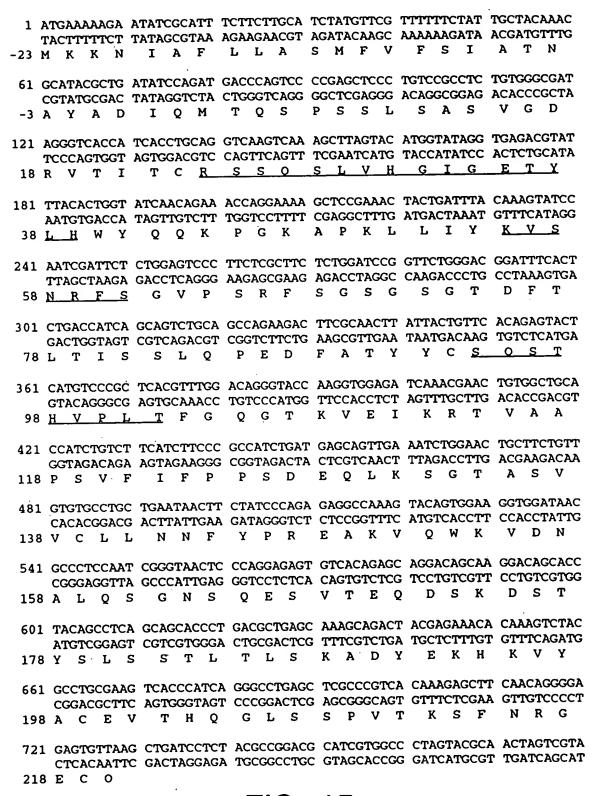
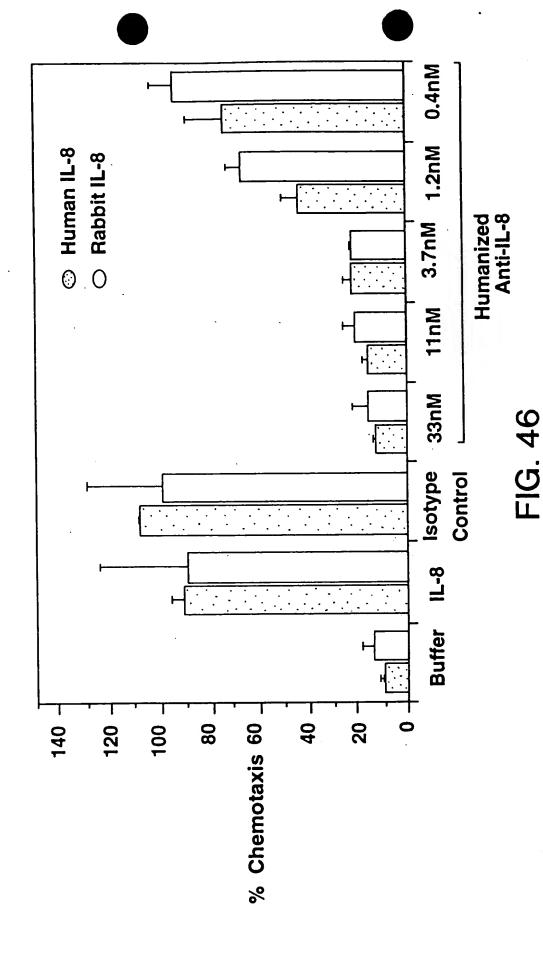


FIG. 45



N35AH1upr

5'-CTAGTGCAGTCTGGCGGTGGCCTGGTGCAGCCAGGGGGCTCACTCCGTTTGTCCTGTGCAGCTTCTGGCTACTCCTTC-3

N35AH1lwr

5'-TCGAGAAGGAGTAGCCAGAAGCTGCACAGGACAAACGGAGTGAGCCCCCTGGCTGCACCAGGCCACCGCCAGACTGCACT AG-3'

Bold indicates nucleotide change destroying Pvull site.

FIG. 47

```
> length: 8120 (circular)
>This has the pSVI backbone with the pRK7 cloning linker (pSVI7) and the intron DHFR(ID)
>made from pSVI.WTSD.D by adding a linearization linker(LL) into the Hpal site
  > /home/ruby/vc/Immblo/afan/ss.p6G425v11.N35A.choSD > sites: std
> Wed May 7 18:27:36 1997
```

			Tarca	1179	mva.l	TIOCO	7 11000	A 1990	INTER	[ + B	י יייטטן דעקעס	DBBOT	hampi nlaiv cac81	<b>ないかられてい こうかい こうかい こうかい こうかい こうかい こうかい こうかい こうか</b>	TOTOGORANGE CONTRACTOR CONTRACTOR
			sau3AI aluI	mbol/ndeII[dam-]		apir (agii t	pvul/bspCI		r menitride tatd	hinfI taqI[dam-]	rmal mcrl pvull	10.07		bfaI taqI[dam-]	THE CACTIFORM ATTAINED ATTAINED A SEAGLOGATO GACAGOTOTO GAATGIGIGI CACTIFOCOCT GIGGAMAGIC COCCASOCTO GACAGOTOCTOCTOCTOCTOCTOCTOCTOCTOCTOCTOCTOCTOC
cac8I	aluI	BBtI	Saci	111	110161	hq1AI/aspHI		11001100	bsp1286	beinkal		7 Jun 2 4	banII	tool	<b>正女 じかかなしなじしし じじゅうじゅうじゅう</b>

TICGAGCICG CCCGACAITG ATTAITGACT ANABACTAG CIGTCGACAC CITACACACA GICAATCCCA CACCITICAG GGGICCGAGG GGICGICGG AAGCICGAGC GGGCIGIAAC TAATAACIGA TCICAGCIAG CIGTCGACAC CITACACACA GICAATCCCA CACCITICAG GGGICCGAGG GGICGICGGI	sfaNi ppulOI ns11/avalII	nlalli sphi nspi
GTCAATCCCA		7
AC CTTACACACA	BCLFI mval	dsav bstni
CTAG CTGTCGAC	BCFFI	ecorii deav
SA TCTCAG		
TAATAACT	H.,	ıvalıl
GGGCTGTAAC	sfaNI ppul0I	· nsil/avalli nlalli sphi
TTCGAGCTCG AAGCTCGAGC		

101 GAAGTATGCA AAGCATGCAT CTCAATTAGT CAGCAACCAG GTGTGGAAAG TCCCCAGGCT CCCCAGCAGG CAGAAGTATG CAAAGCATGC ATCTCAATTA CTTCAATTAT AGGGTCCGC GGGTCGTCC GTCTTCATAC GTTTCGTACG TAGAGTTAAT CTTCATACGT TTCGTACGTA GAGTTAATCA GTCGTTGGTC CACACCTTTC AGGGGTCCGA GGGGTCGTCC GTCTTCATAC GTTTCGTACG TAGAGTTAAT bsmFI nlaIV cacel

nlaIII

BtyI ncol

IHdeu cacel napi

cacel

apyI[dcm+]

beaJI

apy1[dcm+]

IHdsu

nspI

BexAI

betni deav

acti beaJi bell deal acil bari acil acil fokl acii

201 GTCAGCAACC ATAGTCCCGC CCCTAACTCC GCCCATCCCG CCCCTAACTC CGCCCAGTTC CGCCCATTCT CCGCCCCATG GCTGACTAAT ITTTTTATT CAGTCGTTGG TATCAGGGCG GGGATTGAGG CGGGATTGAG GGGGGTCAAG GCGGGGTAC CGACTGATTA AAAAAAATAA CAGTCGTTGG TATCAGGGCG GGGATTGAGG CGGGATTGAG GGGGGTCAAG GCGGGGTAC CGACTGATTA AAAAAAATAA

haeIII/pall mcrI eagl/xmall1/eclXI eael cfrI bsiEI mspI hpall TATCGG	nlaiii TCATGGT AGTACCA TG^	real csp61 scal AGTACTTC
aluI rmaI rmaI maeI bfaI nheI cacBI aluI CAAAAAGCTA GCT	fnu4HI bsoFI bbvI nspBII aclI ATCCCGCTG CCATCA TAGGGCCGAC GGTAGT	xmnI asp700 ggaacgagtr caa ccrtgcrcaa GTT
rmai maei styi bsaji blui rmai eag avril[dam-] haeili/pali hai stul haei maei cacgi mspi mal bfai alui hpai TTTGGAGGC TAGGCTTTTG CAATAGGCC AAACCTCCG ATCCGAAAAC GTTTTTCGAT CGAATAGGCC	fnu4HI bsoFI bsoFI csal csp61 scfl mnli gTACCGCCTA TAGAGCGATA AGAGGATTTT ATCCCCGCTG CCATCATGCT CATGCCGCAT ATCTCGTAAAA TAGGGGCGAC GGTAGTACCA DHFR ATG^	haelli/pall hael scrFI mval bsrBI ecoRII dsav bstNI acil l apyl[dcm+] bsaJI mnll ddeI cCTACCCTGG CCTCCCTCA
mnli mnli bseRI SAGAGGCTTT	maeli maelii AGTGACGTAA TCACTGCATT	bsmal bsal GGGATTGGCA AGAACGGAGA
fnu4HI bsoFI bsoFI bsoFI bsoFI bsoJI bsaJI ballI/palI haeIII/palI haeIII/palI mnlI bsaJI mnlI haeII bsJI mnlI bsaJI mnlI haeII haeIII/palI mnlI bsaJI acil cacGCCTCT GAGCTATTCGG ATACGAGCCGC GAGCCGGAGA TCCTCCGAAAAC GTTTTTCGAT CGAATAGGCC	tfil hinfi acil thai thai fuuDil/mvni bstUi bsh12361 A GGGGATTCC CGTGCCAAG TT GGGCCTAAGG GGCACGGTTC	haelli/pali hael scrFI scrFI mval bsrBI ecoRII dsav pflMI bslI bsmFI rcGACCATTG AACTGCATCG TCGCCGTGTC CCAAAATATG GGGATTGGCA AGAACGGAGA CCTACCCTGG CCTCCGCTCA AGCTGCTAC TTGACGTAGC AGCGCACAG GGTTTTTATAC CCCTAACCGTT TCTTGCCTCT GGATGGGACCGAGT
fnu4HI bsoFI bglI sfiI haeIII/palI ddeI mnlI mnlI haeIII/palI aluI mnlI bsaJI acil haeIII/palI stargaaga ccaagaccac crcacactar agactatrc agaagataara rccaaaa Atacgreec agaccaaa crcataaa	BCIFI  nc1I  mspI  hpaII  dsaV  cauII  401 CCGGGAACGC TGCATTGGAA  GGCCCTTGCC ACGTAACCTT	taqI S01 TCGACCATTG AACTGCATC AGCTGGTAAC TTGACGTAG

### FIG. 48B

tru9I mseI ahaIII/draI TTTAA	TTGA	I CTTT SAAA
eco571  ecoRII  ecoS71  mboli  earl/ksp6321  mnli  caadGamGamCorc Trcagreaa actregreat ataceatic truges  caadGamara caraacara actregreat ataceatic truges  caadGamara caraacara actregreat ataceatic truges  ecoRII  das truges  tfil  trug  abali  abali  caadGamagaar caaccrtraa  craadGamagaar caaccrtraa  craadGamagaar caaccrtraa	trugi aflii/bfri sfani msei gargccttaa gacttattga ctacggaatt ctgaataact	haell/pall hael hael mval mval ecoRII dsav tfil dsav bstNI nlaIII bstNI ddel plel apyl[dcm+] hinfl apyl[dcm+] hinfl ccAGGAAGCC ATGAATCAAC CAGGCCACCT TAGACTTTT GGTCCTTCGG TACTTAGTTG GTCCGGTGGA ATCTGAGAAA
scrfi mvai ecoRii dsav bstNi apyi[dcm+] exAi ccTGGT TCTCCATTCC I GGACCA AGAGGTAAGG A	sstI sacI hgiJII hgiJII hgiJII hgiJII hgiJII hgiJII bspl286 bs	ha scrFI mval ecoRII tfil dsav nlaIII bstNI m+) hinfi apyI( NGCC ATGAATCAAC CAG
acrFI mvaI ecoRII dsav bstNI apyI{d sexAI s AAAACCTGGT	PHI bs: T TTCTTGCCA A AAGAACGG	
TATGGGTAG	ssti saci hgiJii hgiAI/aspHi ecll36Ii bspl286 bslHKAI bmyI mnli aluI si banII bseRI GA GGAGCTCATT T	GTTCTGTTT) CAAGACAAA
tfil hinfi hphi alwwi[dcm-] caga atctggtat gtct tagaccacta	s s h h h e e e b mull bsssi b bsli bseki Accaccaca GG	mnli GTCGGAGGCA CAGCCTCCGT
tfii hinfi alwwi ( GGTAAACAGA A	AACTCAAAGA	II GGTTTGGATA CCAAACCTAT
eco571 mbo11 nb1 crc rrcAGTGGAA	dde1 CTCAGTAGAG	acci nlaili AAGTAGACAT GG
eco57 mboli earl/ki mnli ccacaacctc TTG	tru9I ddeI mseI asi/asnI/vspI aggacagaat taatatagtt ctcagtagag aactcaaaga	mspi hpaii bsawi acaaccgaa ttggcaagta aagtagacat ggtttggata gtcggaggga gttgtgttta tgttggcctt aacgttcat ttcatctgta ccaaacctat cagcctccst caagacaat
CAAAGAATGA	tr ma me AGGACAGAAT TCCTGTCTTA	mspi hpali bsawi 801 acaaccggaa ttggcaagta aagtagacat ggtttggata gtcggaggca gttctgttta tgttggcctt aaccgttcat ttcatctgta ccaaacctat cagcctccgt caagacaaat
601	701	801

### FIG. 48C

hinli/acyi

hgai

```
bell ddel
                                                                                                                                                      901 GIGACAAGGA ICAIGCAGGA AITIGAAAGI GACACGIIII ICCCAGAAAI IGAIIIGGGG AAAIAIAAAC CICICCCAGA AIACCCAGGC GICCICIG
                                                                                                                                                                         CACTGITCCI AGTACGICCI TAAACIIICA CIGIGCAAAA AGGGICIIIA ACIAAACCCC IIIAIAIIIG GAGAGGGICI IAIGGGICCG CAGGAGAAC
                                                                                                                                                                                                                                                                                                                                                                                   1001 AGGTCCAGGA GGAAAAAGGC ATCAAGTATA AGTTTGAAGT CTACGAGAAG AAAGACTAAC AGGAAGATGC TTTCAAGTTC TCTGCTCCCC TCCTAAAGCT TCCAGGTCCT CCTTTTTCCG TAGTTCATAT TCAAACTTCA GATGCTCTTC TTTCTGATTG TCCTTCTACG AAAGTTCAAG AGACGAGGG AGGATTTCGA
                                                                                              ecoNI
ahall/bsaHI
                                       mnll
                                                                                                                    apyI[dcm+]
                                                                                                                                                                                                                                                                                                                                                                     mnlI
                                                          ecoRII
                     BCLFI
                                                                                                betNI
                                                                              dsav
                                        mval
                                                                                                                                      bsaJI
                                                                                                                                       mn]I
                                                                                                                                                                                                                                                                                                                                                                     Ilodm
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        bsaJI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                     · styI
                                                                                                                                                                                                                                                                                                                                                                      accI
                                                                                                                       afllii
                                                                                                                                      maeIII
                                                                              mbol/ndeII[dam-]
                                                                                                                                                                                                                                                                                                                                                                      sfanı
                                                                                                                                          maeIII alwI[dam-] apoI
                                                                                                                      dpnII[dam-]
                                             nlallI
                                                                                                    dpnI (dam+)
                                                              sau3AI
                                                                                                                                                                                                                                                                                                             apyI[dcm+]
                                                                                                                                                                                                                                                                                                                                                                        mnlI
                                                                                                                                                                                                                                                          ecoRII
                                                                                                                                                                                                                   scrFI
                                                                                                                                                                                                                                                                            dsav
                                                                                                                                                                                                                                                                                               batNI
                                                                                                                                                                                                                                       mval
                                                                                                                                                                                                                                                                                                                                     Bau96I
                                                                                                                                                                                                                                                                                                                                                      avall
                                                                                                                                                                                                                                                                                                                                                                          asuī
```

ecoRII

SCLFI mvaI

ATGCATITIT ATAAGACCAT GGGACTITIG CTGGCTTTAG ATCCCCTTGG CTTCGTTAGA ACGCAGCTAC AATTAATAC TAACCTTATG TATCATACAC TAACGTAAAA TATTCTGGTA CCCTGAAAAC GACCGAAATC TAGGGGAACC GAAGCAATCT TGCGTCGATG TTAATTATGT ATTGGAATAC ATAGTATGTG

sau96I avall asuI

asel/asnl/vspl

tru9I mseI

fnu4HI

mbol/ndeII[dam-]

8au3AI

dpnII[dam-]

cacBI

dsal bsmFI

beaJI

nsil/avallI

1101

nlaIII

styl ncol

dpnI[dam+] alwi[dam-] bstYI/xhoII

**bsoFI** bbvI

ecoRI taqi apoI c clai/bsp106 II bspDI[dam-] rCGGTTCTAT CGATTGAATT AGCCAAGATA GCTAACTTAA	scrFI mval fnu4HI ecoRII dsav bstNI bsoFI apyl(dcm+) haeI bbvI acii haeIII/pali TCTGGCGGTG GCCTGGTGCA AGACCGCCAC GGACCACGT	ecrFI  ncii mspi hpali dsav cauli xmal/pspAi smal smal smal smal smal smal smal smal
dsav tagi ecoRI bstNI tagi apol apyI(dcm+) mnli clai/bspl06 hphi scfi fokI bgTGACACTT TAGATTGCC TTTCTCTCCA CAGTGTCCA CTCCCAGGTC CAACTGCACC TCGGTTCTAT CGATTGAATT CCACTGTGAT ATCTATTGTA GGTGAAACGG AAAGAGAGT GTCCACAGGT GAGGTCCAG GTTGACGTGG AGCCAAGATA GCTAACTTAA seq from pRK6G425VH: Cla-AvrII^	rmal mael bfal alul cAGAAGTTCA GCTAGTGCAG GTCTTCAAGT CGATCACGTC	sau96I sau96 avali nlaIV asuI nlaIV bsrI TATGCACTGG GTCCGTC ATACGTGACC CAGGCAG
beli TTTCTCTCCA CAGGTGTCCA ( AAAGAGAGGT GTCCACAGGT	nlaili styi pfimi ncol dsai bsli foki maei bpmi/gsul[dcm-] bsai csp6i ccaccargGG arggrcargr arcarcctr trctagragc aactgcaact ggagracatt c	pleI hinfI taqI xhoI paeR7I avaI maeIII avaI maeIII x S F S S H Y Y S F S S H Y FIG. 48E
maeiii hphi scfi foki ggtgacacta tagataacat ccactttgcc ccactgtgat atctattgta ggtgaaacgg	rmel meel I foki bfal ATCATCCTIT TTCTAGTAGC TAGTAGGAAA AAGATCATCG	hgiJii bapi286 bmyi bmyi mval banli ecoRii dsav bstNi bstNi bsaJi apy1[dcm+] ccacgcgcc rcacrccgrr rgrccrgrgc Actrcrgcc cgcrccccc AgrasGcAA ACAGGACACG p G G S L R L S C A A S G
maeIII hphi scfi 1201 atacgattta GGTGACACTA TATGCTAAAT CCACTGTGAT	nlalli styl pflMI ncol dsal bsal fokl nlalli fokl 1301 CCACCATGG ATGTCATGT GGTGGTACCC TACCAGTACA TAGTAGGAAA	hgiJII bep1286 bmyI bmyI bmyI ecoRII deav bstNI bsaJI apyI dcm+} 1401 GCCAGGGGC TCACTCCGTT CGGTCCCCG AGTGAGGCAA

		~
thai fnuDII/mvnI haeIII/pali batui aaugi nrui GTTCAAGGC CGTTTCACTT TATCTCGGGA CAACTCCAAA AACACAGCAT CAAGTTCCC GCAAGTGAA ATGAGGCT GTTGAGGTTT TTGTGTCGTA	hinli/acyl ahali/beahi beri aatli maelii taqi hphi mboli maeli r CAATGGTGAC TGGTTCTTCG ACGTCTGGGG	sau961 sau961 nlaly hgiJii hgiCi bani bap1201 bap1201 banii mvai agui mvai agui mvai agui mboli ecoRii agui bali/pali batii bap1286 styl haelli/pali batii bap1286 styl haelli/pali batii bayi[dcm+] mnli bayi mnli bayi nspBii apyi[dcm+] II/pali ecoOl091/drali basi mnli bayi mnli bayi mspBii apyi[dcm+] CTCCACCAAG GGCCATCG TCTTCCCCT GCACCCCC GTGTCGCGC GAGGTCTTC CCGGGTAGCC AGAAGGGGGA CGCTGGGGG CACAGCGGCC GAGGTCCTTC CCGGGTAGCC AGAAGGGGGA CGCTGGGGG CACAGCGGC GAGGTCCTTC CCGGGTAGCC AGAAGGGGGA CGCTGGGGGA AGGTTCTCGT GGAGACCCC GTGTCGCCG GAGGTCCTTC CCGGGTAGC AGAAGGGGGA CGCTGGGGG CACAGCGGCC GAGGTCCTTC CCGGGTAGC AGAAGGGGGA CGCTGGGGGA AGGTTCTCGT GGAGACCCC GTGTCGCCG GAGGTCCTTC CCGGGTAGC AGAAGGGGGA AGGTTCTCGT GGAGACCCCC GAGGTCCTTC CCGGGTAGC AGAAGGGGGA CCGTGGGGGA AGGTTCTCGT GGAGACCCCC GAGGTCCTTC CCGGGTAGC AGAAGGGGGA CCGTGGGGAG AGGTTCTCGT GGAGACCCCC GAGGTCCTTC CCGGGTAGC AGAAGGGGGA CCGTGGGGAG AGGTTCTCGT GGAGACCCCC GAGGTCATC CCGGGTAGC AGAAGGGGGA CCGTGGGAGG AGGTTCTCGT GGAGCCCCC GAGGTAGCTTC CCGGGTAGCGGGA CCGTGGGAGG AGGTTCTCGT GGAGCCCCC GAGGTAGTCTTC CCGGGTAGCTTCCCT GGAGCCCTAGGGGGAG AGGTTCTCGT GGAGCCCCC GAGGTAGTCTCCCT GGCCACCCTC TCCAAGAGGGGAG AGGTTCTCCT GGAGCCCCC GAGGTAGTCTTC CCGGGTAGCTTC GGAGCCCCC GAGGGTAGCCTTC CCCAAGAGGGGAG AGGTTCTCCCT GGAGCCCCC GAGGTAGTCTCCCT GGCCACCCTCC TCCCAGGGGGAG AGGTTCTCCCC GTGTCCCCCC GAGGTAGTCTTCCCCT GGCCACCCCCC GGGTAGCCCCCCCCCC
thai fnuDII haeIII/pali betUI betUI betUI sau96I nruI cTTCAAGGGC CGTTTCACTT TATCTCGCGA CAAGTGAA ATAGAGGCT F K G R F T L S R D	mnli GCAAGAGGG ATTATCGCTF CGTTCTCCCC TAATAGCGA1 A R G D Y R Y	nlalv ban! scrf! mva! mva! mbol! ecok!! bpuA! dsav bsek! l/pal! bstN! bsek! l/dral! bstN! mnl! carcgc rctrcccct ggcaccrcc ggracc agaagggga ccfggaga c
	rgccgt ctattactgt acggca gataatgaca a v y c	sau961 sau961 nlaiv hgiJII bap1201 bap1201 banII mboII asuI apaI bpu i styI haeIII/palI haeIII/palI ecol091/draII ccc caccacaa Gcccarccc a s r k g p s v A S r k G p s v
beli eau3Ai mbol/ndeli[dam-] dpni[dam+] alwi[dam-] hphi ATATTGATCC_TTCCAATGGT GAAACI I D P S N G E T	cac81 mnl1 cac81 ddel drd1 GAACAGCCTG CGTGCTGAGG ACAC CTTGTCGGAC GCACGACTCC TGTGI	esp31  scrF1 mval bsmB1 ecoRII dsaV dsaV apy1(dcm+) bsaJ1 bsaJ1 mseIII bseRI mn. C CTGGTCACC TCTCCTCGGC GG GACCAGTGGC AGAGGAGCCG IL V T V S S A
1501 TGGGTTGGAT ACCCAACCTA 47 W V G Y	scfI pstI bspMI bspMI 1601 ACCTGCAGAT TGGACGTCTA 81 L O M	nlali 1701 TCAAGGAA AGTTCCTT

មកិតិច	<b>⊄</b> ₩	r G G D J I
I GCTGTCCTP CGACAGGAI A V L	I CACA AGCCCAGCA GTGT TCGGGTCGT H K P S N ahdi/eamll051	mboli bpuAl bbsi mnli GTCAGTCTTC CAGTCAGAG S V F
mspI hpaII scrFI nclI nol dsav snol cauli ACCTTCCCG G	tfil hinfi il grgaarcaca cacrragigr v n H K ahdi/	scrfi mval asul ecoRII dsav bstNI nlaIV bsaJI bsmFI apyI[dcm+] cc TcGGGGGACC iG ACCCCCTGG
hinp!  hill hall acil apall/shoise Gettectace Gettectace Centered	BACCATCTGCAAC GTAGACGTTG I C N	15. J
hinp!  alv  nar!  bi  hinll/acy!  hgic!  hae!!  ban!  aha!!/beaH!  dde! hha!/cfo! nsp  CTCAGGC GCCCTGACCA  GAGTCCG CGGGACTGGT  S G A L T S	ddel plei fnudHI rmai bsoFi nlaIV mnli hinfi bsoFi bspl286 mael bani eco811 bbvi maeIII bfal alui bspl286 bsu36I/mstII/saul ddel hphi bmyl mnli bbvi bmyl AGTCCTCAGG ACTCTACTCC CTCAGCAGCCG TGGTGACTGT GCCCTCTAGC ACTTTGGCCA CCCAGACCTAA TCAGGAGTCC TGAGATGAGG GAGTCGTCGC ACCACTGAGATGAGG GAGTCGTCGC ACTTGGCCAT TCGAGACTCG TGGAGATGAGG GAGTCGTCGC ACCACTGACAT TCAGGAGTCG TGAGATGAGG GAGTCGTCGC ACTTGAGATGAGG GAGTCGTCGC ACCACTGACAT TCAGGAGTCG TGAGATGAGG GAGTCGTCGC ACCACTGACAT TCAGGAGTCG TGAGATGAGG GAGTCGTCGC ACCACTGACAT TCAGGAGTCC TGAGATGAGG GAGTCGTCGC ACCACTGACAT TCAGGAGTCC TGAGATGACGC ACCACTGACTCT ACCACTGAAT TCAGGAGTCC TGAGATGAG GAGTCGTCGCAT ACTTAGAGTCC TGAGATCGCT GGGTCTTGGAT TCAGGAGTCC TGAGATGAG ACTTAGAGTCC ACCACTGACTAA ACTTAGAGATGAG ACTTAGAGAGTCC TGAGACCCTAA ACTTAGAGATCGCAAT TCAGGAGTCCTAGAAT ACTTAGAGATCC TGAGACCCGT GGGTCTTGGAT TCAGGAGTCC TGAGATGAG ACTTAGAGATGC ACCACTGGAAT ACTTAGAGATCGCAAT ACTTAGAGATCGCAAT ACTTAGAGATCGCAAT ACTTAGAGATCGCAAT ACTTAGAGATCGCAAT ACTAGAGATCGCAAT ACTAGAGATCGAAT ACTAGAGATCGCAAT ACTAGAGATCGAAT ACTAGAGATCTAGAGATCGAAT ACTAGAGATCGAAT ACTAGAGATCAAT ACTAGAGATCAAT ACTAGAGAAT ACTAGAGATCAAT ACTAGAGATCAAT ACTAGAGATCAAT ACTAGAGATCAAT ACTAGAGATCAAT ACTAGAGATAAT ACTAGATAAT ACTAGAGATAAT ACTAGATAAT ACTAGATA	
	fnutHI bsoFI  II bsoFI hgiCI II aluI bsp1286 bbvI bbvI cc AGCTTGGGCA cc cc TCGAACCCGT c c C C	hgijii nlaili bapi286 baaji bmyi bmyi maelli nspli nspli caccacge caccacacacacacacacacacacacacacacacacac
maeIII hphI mspI hpaII cfr101/bsrFI bsawI ageI tth1111/aspI GAACCGGTGA CGCTGTGGCCCCCCCCCCCCCCCCCCCCC	fnu4H bsp1286 mael LI bfal al bmyl mnll bbvI crgr gcccrcracc ac	II nd
	DE MACIII hphi bm TGGTGACTGT ACCACTGACT	maeiii A ATCTTGTGAC F TAGAACACTG S C D
bali CTACTTCCCC GATGAAGGGG	fnu4HI bsoFI bsoFI c ddel c cTCAGCAGCG G GAGTCGTCGC L S S V	hgiJii bep1286 bmyi banii TTGAGCCCA?
BGTFI  mval  ecoNI  dsav  batNI  ball  apyl{dcm+}  fnu4HI  bbor  CTGGGCTGC TGGTCAAGGA CTACTTCCCC  GACCCGACGA ACCAGTTCCT GATGAAGGGG  L G C L V K D Y F P	ddel plei mnli hinfi eco811 bsu36/mst11/saul ccrcaGG ACTCTACTCC GGAGTCC TGAGATGAGG	hgijii beaji bepl286 beaji bmyi meli caccaaggig gacaagaaag tigagcccaa giggilocac cigitcitc aacicggii I K V D K K V E P K
1801	1901	2001

nlalli nspl  I nspli mall maelli /mstli/saul GCTCACATGC GTGTGGTG ACGTGAGCCA GCATGTAGG V T C V V D V S H E D P E V K F	real cap61 real maell hphl cap61 beall hgal mol1 AGTACAACAG CACGTACCGT TCATGTTGTC GTGCATGGCA Y 8 V L T V	fnu4HI bBOFI bbvi AGCCCCC ATCGAGAAA CCATCTCCAA AGCCAAAGGG TCGGGGG TAGCTCTTT GGTAGAGGTT TCGGTTTCC A P I E K T I S K A K G
sau961 nlalv mspi hpail scrFi ncil dsav sau3Al avall mbol/ndell[dam-] all caull and dpnl[dam+] ddel dpnl[dam+] bau361 ATGATCTCCC GGACCCTGA TACTAGAGG CCTGGGACT	acil thal thal funDII/mvnI bstUI bstUI bsh12361 sacII/sstII nspBII kspI dsaI bsaJI acil fuu4HI mnlI bsoFI bseRI bartargccaa GACAAAGCC GGGAGGAGC TATTACGTT CTGTTTCGC GCCTCCTCG N A K T K P R E E Q	real bemål mnll csp61 beal band mnll grachagrec aagetereea acanaageeer eec cargineae treeagas and the properties of the
nle real mboli styl mnli 2101 crcrrcccc caalaccaa ggacaccrc agaaaggag Grrrrgccrc caalaccaa ggacaccrc agaaggag gacaccrc agaaggag gacaccrc agaaggag grrrrggar crtrrggag r r r r r r r r r r r r r r r r r	maeli rsal csp6i bsrl bsaAi 2201 TCAACTGGTA CGTGGACGTGC AGTTGACCAT GCACCTCCACG	scrFI mvaI ecoRII dsav ecoNI bstNI bsrI bslI apyI[dcm+] 2301 CCTGCACCAG GACTGGCTGA ATGGCAAGGA GGACTGGCT TACCGTTCCT 314 L H Q D W L N G K E

FIG. 48H

BCLFI mval ecoRII dsav bstNI apyl(dcm+) bspMI ACTGGCGA CCAGTTTCCGA T C L V K G F Y P S	pleI hinfi nlaIV mboII scfI cac8I GGACTCCGAC GGCTCCTTCT TCCTCTACAG CCTGAGGCTG CCGAGGAAGA AGGAGATGTC D S D G S P F L Y 8	Bapi mboli mnli eari/ksp6321 crccacaacc actacaccca gaagacctc gacgrgrrgg tgargrgcgr ctrcrcggag L H N H Y T Q K B L
BGIFI  DOLI  DOLI  DOLI  DOLI  DOLI  DOLI  DOLI  SCRI  SCRI	mapl hpall hpall flud4H  ball ball ball barDl bbvI  ccacatcc ccccccccccccccccccccccccccccc	mboli nlalili bpual ppualo

		/I [dam-]	-
	maeii Aatggttaca Ttaccaatgt	nlalil alwi[dam-] ATCATGTCTG TAGTACAGAC	mbol/nderi[dam-] dpni[dam+] dpni[dam-] dpni[dam-] pvu/bspCI mcri bsiEi taqi[dam-] tru9I clai/bspl06[dam-] bspDi[dam-] mseI bspDi[dam-] mseI bspDi[dam-] aseI/vspI dpni[dam-] aseI/vspI dpni[dam-] aseI/vspI clai/dam-] aseI/vspI dpni[dam-] aseI/vspI clai/dam-I aseI/vspI dpni[dam-] aseI/vspI clai/dam-I aseI/vspI dpni[dam-] aseI/vspI clai/dam-I acc65I clai/dcan-I clai/dam-I clai/dam-I clai/deli clai/d
	eluI fnu4HI bsofI bbvI ACTTGTTTAT TGCAGCTTAT AATGGTTACA TGAACAAATA ACGTCGAATA TTACCAATGT	mael mael 1801 aataaagcaa tagcatcaca ataaagcatt titttcactg cattctagtt giggittgic caaacicatc aatgtagtt atcaggeg Tiatticgtt atcgtagtgi taaagtgit tatticgtaa aaaagtgac giaagaicaa caccaaacag gittgagtag tiacatagaa tagtacagac	mnli ddel acii crga ggcggaaga
* [ ]	ACTTGTTTAT TGAACAAATA	CAAACTCATC GTTTGAGTAG	real csp61 nla1v kpn1 hg1c1 ban1 asp718 macc651 dde1
	acii nasiii/paii fuudhi asui bsoFi nlaili fii styi ei ncoi ri dsai aeili/paii bgil bsaJi sccc ccarcccc ACTT	GTGGTTTGTC	ri c c kp hg ba as crtggttagg
	acii ni fuuddi ai bsofi nlai; sfii styi caei ncoi cfri dsai alui haeiii/pali hindiii bgli baaji SA AGCTTGGCG CCATG	rmai maei bsmi bfai ATAAAGCATT TTTTTCACTG CATTCTAGTT TATTTCGTAA AAAAAGTGAC GTAAGATCAA	mnli Gaaagaggaa Ctitciccit
	taqi plei rmai sali scfi maei hincii/hindii i hinfi psti I/pali bsgii hi crragagrc Gaccrgcaga	be TTTTTCACTG AAAAAGTGAC	pali mnli AATAACCTCT TTATTGGAGA
	tagi plei rmai sali scf. maei hincii/hin maei hinfi pst. haeiii/pali bspMi ig cccragacc Gaccre icc ggarcrea creso	ATAAAGCATT TATTTCGTAA	I hael styl ncol dsal haelli/pall ol nlalli bsajl RC CATGGCCTGA AAT
	BBU hae AGTGCGACGG TCACGCTGCC	apol Ca aatttcacaa Gt ttaaagtgtt	fnu4HI haeI bsoFI styI bbvI ncoI hinPI dsaI hae hhaI/qfoI nlaIIII I/vspI bsaJI GCGCGAGCAC CATGGC
	ecrFI plei foutHI agui nation plei beofinitation nation na	BÍBNÍ BPOÍ AATAAAGCAA TAGCATCACA AATTTCACAA TTATTTCGTT ATCGTAGTGTT	mbol/ndell[dam-] dpn1[dam+] dpn1[dam-] pvul/bspCI mcrI bslEI taq1[dam-] tru9I cla1/bspl06[dam-] bsoFI styI bspD1[dam-] mseI bbvI ncoI mbol/ndell[dam-] hinPI dsal haeIII/p dpn1[dam+] aseI/asnI/vspI bsaJI dpn1[dam-] aseI/asnI/vspI bsaJI cTAGCTAGCC CTTAATTAAG CCGCGGCTG
	scrFI haelilypari  ncil nati  ncil plei foutHI asul  nspi rmal sali scfI styl  hpall saug61 hinfil/hindil eal ncol  bsmAl saug61 hinfi psti cfri dsal  bsli cauli asul bfal acci bspMi hindili bgli bsaJi  AGGGACAGAG GCCCATGAGTC GACCTGCAG GCTAGGCCC ACTTGTTTAT  AGGGACAGAG GCCCATTTAC TCACGCTGCC GGGATCTCAG CTGGACCGC GGTACCGGGT TGAACAATA	AATAAAGCAA TTATTTCGTT	sau3Al mbol/ndeIl[dam dpnI[dam+] dpnII[dam-] pvuI/bspCI mcrI bs1EI taq1[dam-] tru9 cla1/bspl06[dam-] bspDI[dam-] mseI sau3Al xmnI mbol/ndeII[dam-] dpnI[dam+] aseI/ GATCGATCGG GAATTAA
	2701	2801	2901

FIG. 48J

### SOLFI  ### PROUNT  ### PROUNT  #### PROUNT  ###################################	nlalv scrFI mval mval ecoRII ecoRII daav bstNI apyi{dcm+} bsaJI bsaJI 1001 TCCCCAGGCTCCC GTCTTCATAC GTCTCCTTG TATCAGGCG GGGTAGGCC GGGGTAGGC GGGGATTGAG accTAACTC GTCTTCATAC GTTTCGTACG TAGACTTAAT CAGTCCTTG TATCAGGCG GGGATTGAG accTAACTC GTCTTCATAC GTTTCGTACG TAGACTTAAT CAGTCCTTG TATCAGGCG GGGGTAGGGC GGGGATTGAG accTAACTC TAGACTTCATAC GTTTCGTACG TAGACTTAAT CAGTCCTTTCG TATCAGGCG GGGATTGAG accTAACTC TAGACTTCATAC GTTTCGTACG TAGACTTAAT CAGTCCTTTCG TATCAGGCG GGGATTGAG accTAACTC TAGACTTCATAC GTCTCAATTAAT CAGTCCTTTCG TATCAGGCG GGGATTGAG GGGGTAGGGC GGGGTAGGCG GGGGTAGGCG GGGGTAGGCG GGGATTGAG accTAACTC TAGACTCCTTCATACTTCATACTCTTCATACTCTTCATACTCCTTCATACTCCTTCATACTCTTTCATACTCTTCATACTCTTTTTT	fnu4HI bsoFI bsoFI bg1I styI ncol bs1I ddeI bs1I ddeI mnll mnll aluI bseRI bseRI cGCCCAGTTC CGCCCCATCT CGACTAAT TITITIATT TATGCAGAGG CCGAGGCGG GAGCCGAGA CTCGATAAGG TCTTCATCACCGCC
sfaNI ppulOI nsil/avalII nlaIII sphI sphI nspI I cac8I GCA GAAGTATGCA AAGCATGCAT	acii bamfi tta gtcagcaacc atagtcccgc	fnu4HI bsoFI bsoFI bslI sf1I haeIII/palI mnlI mnlI bsaJI aciI h rATT TATGCAGGC CCGAGGCGC CTCG
scrFI mval ecoRII dsaV bstNI apyl [dcm+] bsaJI bsmFI nlaIV cac8I GTGGAAAGTC CCCAGGCTCC	efaNI ppulOI nsil/avalII nlaIII sphI nspI nspHI cac8I cacAAGCATGC ATCTCAA GTCTTCATAC GTTTCGTACG TAGAGTT	nlalli styl ncol ball daal acil baaji ccgcccarg GCTGACTAAT TTTTTTTTTTTTTTTTTTTTTTTTTTTT
3001 GAATGTGTGT CAGTTAGGGT	nlalv scrFI mval ecoRII dsav bstNI apy1{dcm+} bsaJI 3101 TCCCCAGGCT CCCCAGCAGG CAGAAGT	nlali styl ncol bsl dsal bsrl acil acil acil bsall 3201 CGCCCAGTTC CGCCCATG

## FIG. 48K

tfil hinfi acil thai thai fuuDil/mvni plei bstui hinfi cccGATTCC CCGTGCCAAG AGTCAGGTAA GCGCCTAAGG GGCACGGTTC TCAGTCCATT U1 matched splice donar^	sau3AI mbol/ndeII[dam-] dpnI[dam-] alwI[dam-] taqI[dam-] clai/bspl06[dam-] bspDI[dam-] sau3AI mbol/ndeII[dam-] dpnI[dam-] dpnI[dam-] TG GAAACCTACTGACAT TTG GAAACCTAG CTAGGATGAC TTG GAAAACTAG CTAGGATGAC TTG GAAAACTAG TG  "Lemoved ATG "Lemoved ATG lariat consensus" IgG vH natural lariat restored^
scrFI ncil mspl hpail dsav haeili/pall ul mcil eagl/xmaili/eclXI eael cfri bsiEI mspl cauli hpail Avril - Hindill frag	fnu4HI bsoFI acii thai thai fnuDII/mvnI tru9I bstUI mseI bsaJI bsh1236I aseI/ashI/vspI ccTTGGCTTC GTTAGAACGC GGCTACAATT AATACATAAC GGAACCGAAG CAATCTTGCG CCGATGTTAA TTATGTATTG ^sp6 promoter
scrFI  ncii  mael  styl  styl  bgaJi  blui  avrii(dam-)  mael  cacli  bfai  cacli  bfai  cacli  mapl cauli  hael  rcccccaaa Aaaccrccgc ArccgaAaAccrtccgc GcGGGAACGc  cacda mapl cauli  hael  alui  mall bfai  alui  haeli  regirom psvi6B5-6G4VL: Avrii - Hindili frag	fnu4HI bsori acii bstxi thai thail/mvni tru9I rsai plei haelII/pali bstUI msel csp6I scfi hinfi asul bsaJI bsh1236i asel/asnl/vspI csp6I scfr hinfi asul bsaJI bsh1236i asel/asnl/vspI csp6GGGT ATCCGGGTGGG GGAACCGAAG CAATCTTGGCTTAA TTATGTATTG catGGCGGAT ATCTCAGATA TCCGGGTGGG GGAACCGAAG CAATCTTGGCGGAT ATTCTAGTATTG catGGCGGAT ATCTCAGATA TCCGGGTGGG GGAACCGAACC

FIG. 48L

fokI I I I I I I I I I I I I I I I I I I	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	CCGAA GGCTT P K
III styl I dsal bsll fok bsall CACCATGGGA	I TCTGT( AGACA( S V	alui h+j AAGCTO TTCGAO
nlaIII  b pflMI  ccoRI d  i apol b  I[dam-]  GATTGAATTC CAC	alui  seti  saci  hgiJii  hgiAl/aspHI ecl136II.  bsp1286  bs1286  bs1286  bs14KAI  bsrI avai  avai  avai  ATGACCCAGT CCCCGAGTC CCTGTCCGCC TV  TACTGGGTCA GGGGCTCGAG GGACAGGCGG AV  M T Q S P S S L S A S	scrfi mvai ecoRII dsaV bstNI aluI apyI[dcm+] GTATCAACAGAA AAGCTCCGAA CATAGTTGTC TTTGGTCCTT TTCGAGGCTT Y Q Q K P G K A P K
clal/bspl06 sfaNi fnu4Hi bsoFi taqi apo bbvi bspbi[dam-] GGGCTGCATC GATTGAA	alui  sati  saci  hgiJii  hgiJiiii  hgiJiiii  hgiJiiii  bsp1286  bsp1286  bsp1286  bsp1286  bsp1286  bsp1286  tthlll/aspi banii  gaccagr cccaacrc ccro	GTATCAACAG CATAGTTGTC Y Q Q
rmal bfal cac81 si alul alui rcGATCGAA	ber beri tth111/ ATGACCAGT TACTGGGTCA H T Q S	BECFI  maeli  BRABI  BRABI  BRAI  BRAI  BRAI  GGTGCTACGT ATTTACACTG GTATCAACAG AACCTCGAA  CCACGATGCA TAAATGTGAC CATAGTTGTC TTTGGGGCTT  G A T Y L H W Y Q Q K P G K A P K
mael thal nhel fnuDII/mvnI betUI beaJI nrul cc TCGGTTCGCG A	rmal rsal maei bpmi/gsul[dcm-] bfal bsrl csp61 ecoRV TCTAGTAGCA ACTGCAACTG GAGTACATTC AGATATCCAG AGATCATCGT TGACGTTGAC TCTATAGGTC	maeli Bnabi bsaai GGTGCTACGT CCACGATGCA G A T Y
I  thi  thi  beal  CAACTGCACC TC  GTTGACGGG AG  GTTGACGGG AG	rsal bpml/gsul[dcm-] srl csp61 crg cactacattc	real [ csp61 [ nlaili AGT ACATGGTATA ICA TGTACCATAT V H G I
sau961 aval1 asu1 scrF1 mva1 ecoR11 dsaV bstNI apy1[dcm+] bsaJ1 CTCCCAGGTC CA	rmal real bpmI/gsul[dcm-] bfal bfal csp61 TCTAGTAGCA ACTGCAACTG GAGTACATTC AGATCATGTAAG	rsal ddel alui csp6) hindili i AAAGCTTAGT AC TTTCGAATCA TG
beli caggrercca ( grccacager (	mal mael bfal rcharaca agarcarcer	psti bsgi rsal see83871 ddel bspMI alul csp61 hphl bspMI hindIII nlaIII CATCACCTGC AGGTCAAGTC AAAGCTTAGT ACATGGTATA GTAGTGGACG TCCAGTTCAG TTTCGAATCA TGTACCATAT ITCRSSQCT
TTTTTCTCCA	foki TCATCCTTT AGTAGGAAA	
Bau96 avaII avaII asuI mvaI mvaI ecoRII dsaV bstNI apyI{dcm apyI{dcm ccactttttc tttttctcca caggectca ctcccaggec ggtgaaaaag aaaagget gtccaggec	nlaIII 3601 TGGTCATGTA ACCAGTACAT	hphi maelii beteii ATAGGGTCAC TATCCCAGTG
3501	3601	3701

### FIG. 48M

fnu4HI bsoFI bbvI fI fI fI fI fC G	HI I I I I I	haeIII/palI aeI 11 GGCCAA CCGGTT A K
fn bb, bb, scfi psti bagi caccagrere GTCGTCAGAC	dam-] fnu4H bsoFI bbvI ACTGTGGCTG TGACACCGAC	haell) hael mnll GAGAGGCCAU CTCTCCGGTF E A K
CTCTGACCAT GAGACTGGTA L T I	Bau3AI mbol/ndell[dam-] fnu4HI dpnl[dam+] baoFI dpnll[dam-] bbvI GATCAAACGA ACTGTGGCTG CTAGTTTGCT TGACACCGAC	TTCTATCCCA AAGATAGGT F Y P R
I ACGCATITCA TGCCTAAAGT I D F I		xmni asp700 scrcaataac scacttaffG L N N
mspI hpall bsli bsawI sau3AI mbol/ndeIl[dam-] dpnI[dam+] dpnI[dam-] alwI[dam-] laIV satYl/xhoII lanH lanH lanH lanH sanH lanH lanH lanH lanH lanH lanH lanH l	real csp61 nlaIv kpnI styI hg1CI banI bsaJI asp718 acc651 GGACAGGGGTA CCAAGGTGGA CCTGTCCCAT GGTTCCACCT G Q G T K V E	CACBI TGTGTGCCT ACACACGGA V C L
mspl hpall bsll bsawl sau3Al mbol/ndell[dam+] dpnl[dam+] alwl[dam-] nlalV bstYl/xholl batYl/xholl banHl crcrgGArc cGGTTC sAGACCTAG GCCAAG	naeli scrcacgiti GG igagigcaaa CC L T F G	ACTECTTOTS T TEACESAGE A T A S V
mspI hpall bsaWI sau3AI mbol/ndell[dam-] dpnl[dam+] dpnl[dam-] alwi[dam-] ldcm-] batxI/xholl banHI ccttctcgct rctctgatctcgc AcgatttcA ctctgacctcGacgacgacgacgacgacgacgacgacgacgacgacgacga	berBI acil bemFI nlaIII CCATGTCCC GC AGTACAGGC CG	xmnI xmnI haeII. haeII. haeII asp700 mnlI asp700 mnlI mnlI crecrecy getgaataac teetgeaagac acceptagae coectaataac eegecaa ceettaata aagatagge ceeteceget x s g T a s v v c L L n n P Y P R E A K F G T A S V V C L L N N P Y P R E A K E A K E A K E C E E N N P Y P R E A K E A K E A K E A K E A K E A K E E A K E E A K E E E E
bsmFI bpmI/gsuI[dcm-] .06 pleI .1 hinfI TCTGGAGTC CCTTCT RAGACCTCAG GGAAGA S G V P S	real csp61 scal cacacacta c GTCTCAT G	
tfil bsmF hinfi bpmI/gsuI claI/bsp106 pleI bspDI(dam-) hinfi TACAAAGTAT CCAATCGATT CTCTGGAGTC ATGTTTCATA GGTTAGCTAA GAGACCTCAG	berbi real acii csp6i bemFi scal nlaili maeli TTATTACTGT TCACAGAGTA CTCATCTCCC GCTCACGTTT AATAATGACA AGTGTTCAT GAGTACAGG CGAGTGCMA	aoii ccccarcts atgascastt gccggtagac tactcgtcaa P P S D E Q L
ACAAAGTAT C TGTTTCATA G	CTTCGCAAC T GAAGCGTTG A F A T	
mspI hpaII bali bali basi abadi abadi dpol/deli[dam*] dpol/deli[dam*] trai banfI banfI alal/baplo6 pleI bapDI[dam*] banfI alal/baplo6 pleI alwi[dam*] banFI bapDI[dam*] banHI clai/baplo6 pleI alwi[dam*] banFI bapDI[dam*] binfI clai/baplo6 pleI alwi[dam*] banFI bapDI dam*] binfI bapDI dam*] binfI clai/baplo6 pleI banHI bapDI dam*] binfI alwi[dam*] banFI bat bar bagDI dam*] binfI alwi[dam*] banFI bat bar bagDI dam*] binfI alwi[dam*] binfI banFI banHI bapDI dam*] binfI banHI banHI bagDI dam*] binfI banHI banHI bagDI dam*] binfI banHI banHI bagDI dam*] binfI banHI banHI banHI bagDI dam*] binfI banHI banH	real csp61 nlalv kpn1 styl bpual bpual csccacaac trattactgt tcacagaga acttcccaac ttattactgt tcacagaga acttcccaac ttattactgt tcacagaga acttcccaac general acttccaac general acttcc	mboli bpual bbal mboli caccarcrgr ctrcarcrfc GTGGTAGACA GAAGTAGAAG p s v F I F
3801 A	3901 0	4001

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4301 GAGAGTGTTA AGCTTGGCCG CCATGGCCCA ACTTGTTTAT TGCAGCTTAT AATGGTTACA AATAAAGCAA TAGCATCACA AATTTCACAA ATAAAGCATT
CTCTCACAAT TCGAACCGGC GGTACCGGGT TGAACAAATA ACGTCGAATA TTACCAATGT TTATTTCGTT ATCGTAGTGT TTAAGTGTT TATTTCGTAA
                                                                                                                                                                                                                                                                                                                                                                                                                                    4201 CTGACGCTGA GCAAAGCAGA CTACGAGAAA CACAAAGTCT ACGCCTGCGA AGTCACCCAT CAGGGCCTGA GCTCGCCCGT CACAAAGAGC TTCAACAGG
                                                                                                                                                                                                                                                                                                                                                                                                                                                     GACTGCGACT CGTTTCGTCT GATGCTCTTT GTGTTTCAGA TGCGGACGCT TCAGTGGGTA GTCCCGGACT CGAGCGGGCA GTGTTTCTCG AAGTTGTCCC
                                                                                                                             TCAIGICACC TICCACCIAT IGCGGGAGGI TAGCCCATIG AGGGICCICI CACAGIGICT CGICCIGICG IICCIGICGI GGAIGICGGA GICGICGIGG
                                                                                                               4101 AGTACAGTGG AAGGTGGATA ACGCCCTCCA ATCGGGTAAC TCCCAGGAGA GTGTCACAGA GCAGGACAGC AAGGACAGCA CCTACAGCCT CAGCAGCACC
                                                              fnu4HI
                                                                                ddeI bsoFI
                                                                                              scfI mull bbvI
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                MV&I
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FIG. 480

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deal hacili/pall
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                                                                                                                                                                                  4401 TITITCACIG CATICIAGIT GIGGITIGIC CAAACICATC AATGIAICIT AICAIGICIG GAICGAICGG GAATIAATIC GGCGCAGCAC CAIGCCIGA AAAAAGIGAC CIAACIAAG CCGCGICGIG GIACCGGACT
                                                                                                                                                                                                                                                                                                                                       4501 AATAACCTCT GAAAGAGAA CTTGGTTAGG TACCTTCTGA GGCGGAAAGA ACCAGCTGTG GAATGTGTGT CAGTTAGGGT GTGGAAAGTC CCCAGGCTCC
                                                                                                                                                                                                                                                                                                                                                  TIAITIGGAGA CITICICCIT GAACCAAICC AIGGAAGACI CCGCCITICI IGGICGACAC CITACACACA GICAAICCCA CACCITICAG GGGICCGAGG
                                                                                                                                                                                                                                                                                                                                                                                                                                                       nepHI
                                                                                                                                                                                                                                                                                                                             DemFI nlaIV
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                                                                                                                                                                                                                                                                                                                                                                                        ppu10I
                                                                                                                                                                                                                                     BCLFI
                                                                                                                                                                          hhal/cfol nlallI
                                                                                                            haei
                                                                                                                                                                                                                                                                                       bathi
                                                                                                                                                                                                                                                                           deav
                                                                                                                                                                                                                                                   mval
                                                                                                                                                                                                                                                                                                               beaJI
                                                                                                                       bsoFI styI
bbvI ncoI
                                                                                                                                                             beaJI
                                                                                                                                                                                                                                                                                                                                                                                                                               BphI
                                                                                                                                                                                                                                                                                                                                                                                                                   nlaIII
                                                                                                            fnu4HI
                                                                                                                                                hinPI
                                                                                                                                                            dpnll[dam-] asel/asnl/vspl
                                                                                                                                                                                                              ^sv40 origin
         mbol/ndeII [dam-]
                                                                                                             tru9I
                                                                                                                          mseI
                                                                                                clal/bsp106[dam-]
                                                                                                                                                                           asp7.00
                                                                                                                                    mbol/ndeII[dam-]
                                                                                                                                                  dpnI[dam+] xmnI
                                     dpnII[dam-]
                        dpnI[dam+]
                                                                                                                                                                                                                                                                                                                                                                                                                                            apyI [dcm+]
                                                                                                             bspDI[dam-]
                                               pvul/bapCI
                                                                                  taqI[dam-]
                                                                        baiEI .
sau3AI
                                                                                                                                                                                                                                                                                                                                                                                                         ecoRII
                                                                                                                                                                            nlalii alwi[dam-]
                                                                                                                                                                                                                                                                                                                                                                                BCLFI
                                                                                                                                                                                                                                                                                                                                                                                                                                                        bead
                                                             MCLI
                                                                                                                           sau3AI
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csp6I
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                                                                                                                                                                                                                                                                                  kpnI
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                                                                                                                                                          rmal
                                                                                                                                                                       maeI
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                                                                                                                                                                                                                                                                                                                                     moli
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cac81 cac81 cac81 bemFI nlaIV cac81 cacalgeard cacarded for caccaded cacarded cacard

apyI [dcm+]

nspHI

I GCTGACTAAT CGACTGATTA	maelli alul STTTTCGAC	scrittes
nlall styl ncol bsll dsal acil bsajl ccGccccATG	rmal mael styl bsaJI bsaJI bluI avII[dam-] haeIII/palI mll stul mnll hael bseRI mnll bfaI adaagragg aggaggctt trigaaggc tragactg	BC haeIII/pali eaeI cfrI bsrI maeII maeIII bsa CACTGGCCGT CGTTTTACAA CGTCGTGACT GTGACCGCA GCAAAACTC GTGACCGCA GCAAAATGTT GCAGCACTGA CCCTTTTGGG
acil bsrl ccccraactc cccccast ggggattgag gcgggtca	pali ddel mnli alul mnli haeli/pali bseRi CTCGGCCTCT GAGCTATTCC AGAAGTAGTG AGGAGGCTTT GAGCCGGAGA CTCGATAAGG TCTTCATCATCA TCCTCCGAAA	bspMI scfI pstI draI bsgI maeIII cfrI sse83871 aluI bsrI TCCTGCAGGT AACAGCTTG CACTGGCCGT CGTA
		ip:   /cfo    /mvn      
acil bsmFI 4701 ATCTCAATTA GTCAGCAACC ATAGTCCCGC TAGAGTTAAT CAGTCGTTGG TATCAGGGCG	fnu4HI bsoFI bgli sfiI haeIII/pal mnli mnli mnli bsaJI tTTTTTTATT TATGCAGAGG CCGCGCGC CTC AAAAAATAA ATACGTCTCC GGCTCCGGCG GAG	fnu4HI haeIII/pall hinp: mcrI eagl/xmalli/eclXI thal eagl/xmalli/eclXI thal eagl/xmalli/eclXI thal eagl cast fnubli barBI bsoFI hinPI taqI cfrI hinPI taqI cfrI hinPI xhoI fnu4HI tru9I cac8I paeR7I bs1EI pacI ascI avaI bsoFI mseI tru9I bsh12: mnlI aciI aciI mseI bssHII 4901 TTACCTCGAG CGGCGCTTA ATTAAGGCGC G AATGGAGCTC GCCGCGTTA ATTAAGGCGC G Alinearization linker inserted in

### FIG. 48Q

sau3AI mbol/ndeII[dam-] dpnI[dam+] dpnII[dam-] vvI/bspCI icrI saiEI GATC GCCTTCCCA ACAGTTGCGT	hinpi thai thai thail/mvni bstUi scfi bsh1236i rsai hhai/cfoi csp6i bsli caACCATAGT ACGCGCGTG	mboli CTTTCGCTTT CTTCCCTTCC
sau9éI haeIII/pall asuI mnll acil p mboII cac8I m car1/ksp6321 b CGAAGAGGCC CGCACG	hinpi thai thai fundii/mvi bstui scii scii scii scii scii scii csp6i bsli GTGCGGTATT TCACACCGCA TACGTCAAAG CAACCATAGT ACGCGCCCTG	hinpi hhal/cfol mal hinpi haeli hhal/cfol bsrBi haeli mael acil cacil bfal cacil GC CAGCGCCCTA GCGCCGCTC
cac8I aluI pvuII nspBII cac8I ACATCCCCCC TTCGCCAGCT GGCGTAATAG	sfaNI acil : TTTTCTCC TTACGCATCT GTGCGGTATT	fnu4HI bsoFI hinPI hhal/cfoI thal thal fnuDII/mvnI bstUI bstUI maeIII bbvI maeIII cac8I cCAATGCGCCACCCTAC GAAGGCGAAA GAAGGGAAAGGGAAAGGGAAAGGGAAAGGGAAAGGGAAAGGGAAA GAAGGGAAA
fnu4HI tru9I bsoFI maeIII mseI bbvI f 5001 TGGCGTTACC CAACTTAATC GCCTTGCAGC AC ACCGCAATGG GTTGAATTAG CGGAACGTCG TG	hinPI hhal/cfoI nlaiv nari kasi hinli/acyl hgiCi bali acii bgli alli/bsali bgli accreargece cergargece tracecarae acii maeli csp6i bsli stean certrace gactace arawangage aargectaga cacecaraa acgecetta	acii fnu4Hi bsoFi thai thai fnuDII/mvnI hhai/cfoi hinPi hhai/cfoi hinPi fnu4Hi bsoFi tru9I acii acii msel bshl236i scocgccc cccccccc cc

### FIG. 48R

AAAC	TGTT	tru9I mBeI ITTAA AAATT	acii Actec TGAGG	ACAGA TGTCT
CCCAAAAAAC GGGTTTTTTG	pleI hinfi GACTCTTGTT CTGAGAACAA	alui sa gctgai yt cgacti	9I I AGCCAACTCC TCGGTTGAGG	NI KI ACII TC CGCTT AG GCGAA
nlaIV hgiCI taqI nlaIV ccTTTAGGG TTCCGATTTA GTGCTTTAGG GCACCTCGAC GGGAAATCCC AAGGCTAAAT CACGAAATGC CGTGGAGCTG	maeli haelil/pali dralii sau961 hphi bsaal asul TTGATTTGGG TGATGGTTC CATCGCCCTG ATAGACGGTT TTTCGCCCTT TGACGTTGGA GTCCACGTTC TTTAATAGTG	tru9] bsli bsli aval ccaaactega acaacattca acctattet titgattiat aaggaitit gccgattic gcctattga cctattaa gctttgact tettgagt teggataga aaactaaata	hgial/aspHI bsp1286 bsiHKal baiHKal bmyl ddel for	sfal mspl hpall scrfl bcll dsav fol caull TCCCGCCA
n h b G GTGCTTTAGG	maeli plei drdi hinfi maeli TGACGTTGGA GTCCACGTTC ACTGCAACCT CAGGTGCAAG	t m haelii/pali G GCCTATTGGT C CGGATAACCA	fn fn bs sfaNI r gcrcrgargc	G GCTTGTCTGC C CGAACAGACG
16 nlaIV CCCTTTAGGG TTCCGATTTA GGGAAATCCC AAGGCTAAAT	maell plei drdi hinf TGACGTTGGA G	r GCCGATTTCG	hgial/aspHI bsp1286 bsiHKal bmyl ddel apaLI/snol rsal alw441/snol csp61 GTGCACTCTC AGTACAATCT	hinPI hhal/cfoI thal thal fuuDII/mvnI batUI jal icc GCCCTGACGG
v 1 86 cccrrragge ggGAAATCCC	TTTCGCCCTT	AAGGGATTTT TTCCCTAAAA		nspBII acii hg ccccrca gccact
nlalv hgiJii bsp1286 bmyi banii ATCGGGGGCT C	II/pall II CATCGCCCTG ATAGACGGTT GTAGCGGAC TATCTGCCAA	bali bali aval acctatctc gggctattct tttgatttat tgggatagag cccgataaga aaactaaata	maell psp14061 tru91 msel TTAACGTTTA CAATTTTATG	acil ccccaacac Gcccaacac
aluI CAAGCTCTAA GTTCGAGATT	haeIII/palI au96I suI GGC CATCGCCCTG	I GGGCTATTCT CCCGATAAGA		hinPI 4HI FI hhal/cfol GC GCCCGACAC CG CGGGCTGTG
mspl hpall nael cfrl0l/bsrFl cac6l cccc cTTTCCCGT	maell haell dralli sau961 bsaal asul cca cgracregec C	bali aval ACCTATCTC TGGGATAGAG	vnI trugI mseI sspI T TAACAAATA	hinpi fnu4Hi bsoFi nlaili hhai/cfoI /aspi bbvi rcarggcrgc GCCCG
mspi hpali nael cfr101/berFl alul banli TTTCTCGCCA CGTTCGCCGG CTTTCCCCGT CAAGCTCTAA ATCGGGGCT AAAGAGCGGT GCAAGCGCCC GAAGGGGCA GTTCGAGATT TAGCCCCCGA	me dre dre bee TGATGGTTCA ACTACCAAGT	ACAACACTCA TGTTGTGAGT	tha! fnuDII/mvnI tru9! apo! tru9! mse! bstU! mse! apo! bsh1236! ssp! caaaaatta acGcGaatt Taacaaata	hin fnu4HI maeIII bsoFI maeII bsrI nlaIII hha bsaAI tth1111/aspI bbvI GCTATCGCTA CGTGACTGGG TCATGGCTGC
mspi hpail nael cfr101 maell cac81 5301 TTTCTCGCCA CGTTCGCCGG	maell hael dralli sau96 hphi bsaall asul 5401 TTGATTTGG TGATGGTTCA CGTAGTGGGC AACTAAACCC ACTACCAAGT GCATCACCG		thal fnuDII/mvnI tru9I apol tru9I msel bstUI mseI apol bsh1236I 5601 CAAAATTTA ACGCGAATTT TAA GTTTTTAAAT TGCGCTTAAA ATT	• •
5301	5401	5501	5601	5701

FIG. 48S

# GLE GLE OF GLE IP GLE HEGE WEREN GLE GLE HEGEN GLE

thal fnuDII/mvnI bstUI bstUI bsh1236I hinPI hhal/cfoI mhoII maeIII/palI fnuDII/mvnI mboII sau96I bstUI bsh1236I bsh1236I cccccaccc AGTATTCTTG AAGACGAAAG GGCCTCGTGA GCGCGCTCCG TCATAAGAAC TTCTGCTTTC CCGGAGCACT	nlaIV acii thai thai thai funDII/mvni batui aatii ddel maeii trcttagacg tcaggtggca ctttggggat Aargataa Aagaatctgc agaaaccc tttacaacg ccttggggat Aaacaataa	mboli earl/kep6321 AAAAGGAAGA GTATGAGTAT TCAACATTTC TTTTCCTTCT CATACTCATA AGTTGTAAAG	hgiAl/aspHI bsp1286 sau3Al bsiHKAI mbol/ndeIl[dam-] dpnI[dam+] bmyI dpnI[dam+] bmyI dpnII[dam-] eco57I apaLI/snoI aAGTAAAAGA TGCTGAAGAT CAGTTGGGTG TTCATTTTCT ACGACTTCTA GTCAACCCAC
thal fnuDII/mvnI batUI bahl236I hinPI hhal/cfoI thal mnlI fnuDII/mvnI batUI ccccccaccacc	CTTTTCGGGG	BBPI ATAATATTGA TATTATAACT	hphi ACGCTGGTGA TGCGACCACT
hphi TTCACCGTC ATCACCGAAA	hinll/acyl ahall/bsahl aatii ddel maeli TTCTTAGACG TCAGGTGGCA	AAATGCTTCA TTTACGAAGT	
nspi nspHI fnu4HI bsoFI bbvI   alui nlaiII mnlI hphI hphI GAGCTGCATG TGTCAGAGGT TTTCACCGTC ATCACGAAA			CTGTTTTTGC
I mnlI TGTCAGAGGT	nlaili trugi rcai msei bspHi TTTATAGGTT AATGTCATGA TAATAGT	rcal bspHI II bsmAI I nlaIII T CATGAGACAA	TTTTGCCTTC AAAACGGAAG
nspl   nspl fnu4HI   bsoFI   bbvI   aluI nlaIII mnlI   GAGCTGCATG TGTCAGAGGT	nlaili tru9i rcai msei bspHi TTTATAGGTT AATGTCATGA	berE acil TGTATCCGC ACATAGGCC	fnu4HI bsoFI acil TTTTGCGGCA
scrFI nc11 mc11 mc11 hpa11 dsav esp31 bsmB1 maeIII bsmA1 bs11 cauII GTGA CCGTCTCCGG		CATTCAATA GTAAGTTTAT	CGTGTCGCCC TTATTCCCTT
maell alul caagererga Grrcgacaer	5901 TACGCCTATT	6001 TTTCTAAATA AAAGATTTAT	6101 CGTGTCGCCC GCACAGCGGG
5801	5901	6001	. 6101

hgial/aspHI bsp1286 tru9I bsiHKAI mseI bmyI ahaIII/draI GAGCACTT TTAAAGTTCT	rsal csp61 bsr1 scal hphl maelll GAGTA CTCACCAGTC	sau3AI  hbol/ndeII[dam-]  dpnI[dam+]  dpnII[dam-]  pvul/bspCI  mcrI  bsiEI  ATGACT CTGACAACGA	
maeli psp1406i hgiAl/aspHI xmnI bsp1286 tru9I asp700 bsiHKAI mseI mboli ccGAAGAACG TTTTCCAATG ATGAGCACTT TTAAAGTTCT GGCTTCTTGC AAAAGGTTAC TACTCGTGAA AATTTCAAGA	real csp61 bsrI scal hphl mae ACACTATTCT CAGAATGACT TGGTTGAGTA CTCACCAGTC TGTGATAAGA GTCTTACTGA ACCAACTCAT GAGTGGTCAG	haeIII/palI eaeI cfrI fnu4HI bsoFI acil acil cata acactGCGGC CAACTȚA	mspl sau3Al nlalv mbol/ndell(dam-) alu1
Bau3AI nspBII sau3AI  mbol/ndeII[dam-] mbol/ndeII[dam-] hgiAI/aspHI  dpnI[dam+] dpnI[dam+] xmnI  bstIl/xhoII dpnI[dam-] alw[dam-] alw[dam-] aciI bstIl/xhoII  caccactcc TTACATCCAA CTGGATCTCA ACAGCGGTAA GATCCTTGAG AGTTTTCGC CCGAAGAACG TTTTCCAATG ATGAGCACTT TTAAAGTTCTCA ACAGCACTT CTAGGAACTC TCAAAAGGGG GGCTTCTTGC AAAAGGTTAC TACTCGAA AATTTCAAGA	acil mcri fnu4HI bsiEi bsoFi TCG GTCGCCGCAT	haeIII/pall mb eaeI cfrI dp cfrI dp pvu. bsoFI bsoFI bbvI ACAGAAAAGC ATCTTACGGA TGGCATGTCATT TATGCAGTG TGCCATTAGG GTTGAATGA GACTGTTGCT TGTCATTACG GTTGAATGAAA GACTGTTGCT TGTCTTTTCG TAGAATGCC ACGTATTGCT AGGTATTGCTTGCTTGCTTGCTTGCTTGCTTGCTTGCTTG	nlalli sau3Al maelli mbol/ndell(dam-) sau3Al
sau3Al nspBII sau3Al mbol/ndeII[dam-] dpnI[dam+] batYI/xhoII dpnII[dam-] irl dpnII[dam-] alwI[dam-] alwI[dam-] crGGATCTCA ACAGCGGTAA GATCCTTGAG AGTTTTCGCC GACCTAGAGT TGTCGCCATT CTAGGAACTC TCAAAAGCGG	scrFI ncil ncil mspi hpali dsav hinli/acyl hgal cauli ahall/bsaHI bcgl cccGTGATGA GGCGGGCAAC GGGCCCGTT CTGTTG	II ACA GTAAGAGAAT TATGCA IGT CATTCTCTTA ATACGT	8 E .
sau3Al ne mbol/ndell  dpn1[dam+] bsrl dpn1[dam-] ig TTACATCGAA CTGGATCTCA AC	acil thai fnuDil/mvni bstui bsh1236i hinPi hhal/cfoi GCTATGTGGC GCGGTATTAT CCCGTGA7	sfani foki nlaiii GC ATCTTACGGA TGGCATGAC	19
be bessi maelli taqi 6201 cacgagtGGG TTACATCGAA GTGCTCACCC AATGTAGCTT	h 6301 GCTATGTGG GGATACACC	8 6401 ACAGAAAAG TGTCTTITC	196n¤8

mbol/ndell[dam-] aluI

sau96I avall

dpnI[dam+]

VspI		•		sau3AI mboI/ndeII[dam-] dpnI[dam+] dpnII[dam-] GA
mspI hpali I scrFI tru91 dsav msel cauli asel/asnI/vspI CTTCCGGCA ACAATTAATA GAAGGCCGT TGTTAATATA	mspl hpall cfrl01/bsrFl IV hphl bsmAl sul[dcm-] bsal GCCGGT GAGCGTGGGT	: AACGAAATAG	tru9I msel tru9I ahaIII/draI mseI ATTTAAAACT TCATTTTTAA TAAATTTTGA AGTAAAATT	sau3AI mbol/n dpn1{d dpn11{ GTCAGACCC GTAGAAAGA CAGTCTGGGG CATCTTTTCT
~	bgli cac81 hau961 cac81 hau11/pall cac81 cac81 cac81 cac81 cac81 cac81 cfr101/berF1 cfr101/berF1 cac111/pall cau11 hau1/cfol hau1 hal/cfol hau1 hau1/cfol hau1 cacargate accaratore carcacaca accacacaca accacacaca accacacaca	plei hinfi milo5i GAGTCAGGCA ACTATGGATG CTCAGTCCGT TGATACCTAC		
		plei hinfi ahdi/eamil05i Gacccc GagrcAG	TATA CTTTAGATTG ATAT GAAATCTAAC	dde.I TCGT TCCACTGA
spi beri tru9i maci AACTATTAAC TGGCGAACTA	cac81 .1 scrtgc rggrrr	ahdi/ea GTAGTTATCT ACACGACGGG CATCAATAGA TGTGCTGCCC	ACCAAGTTTA CTCATATATA TGGTTCAAAT GAGTATATAT	maeli tru9i msei rrraacgi gagrri saarrgca crcaaa
	bgli cac81 sau961 sau961 sau961 cac81 bau11/pall bsri mnli asil asul hpali bsri mnli asul hpali cactgring aggregataa agtrecaga ccacttric greaccacc teccetari teaacacc greaccacc accaana		tru9I mnli meel maelII cctcactgat taagcattgg taactgtcag accaagttta ctcatatata Ctttagattg ggagtgacta attcgtaacc attgacagtc tggttcaaat gagtatatat gaaatctaac	CCAAAT CCC GGTTTA GG
hinpi hhal/o fnu4Hi msti bsoFi avill/i maeli cac8i bsrDi maeli cGACGAGCGT GACACCACGA TGCCAGCAGC AATGGCAACA ACGTTGCGCA GCTGCTCGCA CTGTGGTGCT ACGTTGCCGT	bs san 61 hinPI ast I hhal/cfol CCACTTCTGC GCTCGG	Pall mr ATGGTAAGCC TACCATTCGG	ddel nlaIV mbol/ndeII[dam-] dpnI[dam+] hgiCI tru9I dpnII[dam+] banI mnli m8eI maeIII ACAGATGGCT GAGATAGGTG CCTCACTGAT TAAGCATTGG TAACTGTCAGTC	dam-] nlaIII rcaI bspHI GATAATCTCA TGA CTATTAGAGT ACT
fnu4HI bsoFI maell sfaNi bbvI cgacgaggg gacacgagg aATGGC	sau96I avali asul A AGTTGCAGGA CC T TCAACGTCCT GG	thal fnu4HI haeIII/palI fnu4HI haeIII/palI fuuDII/mvnI bsorI sau96I bstUI bsh1236I bsrDI bsrI asuI cTCGCGGTAT CATTGCAGCA CTGGGGCCAG ATGGGGCCATA GTAACGTCGT GACCCCGGTC TACC	nlalV hgiCi tx bani mnli me iGGTG CCTCACTGAT	rmal mael sau3AI mael sau3AI sau3AI hphI mbol/ndeII[dam-] dpoI[dam+] dpoI[dam+] dpoII[dam-] dpoII[dam-] tru9I bstYI/xhoII alwI[dam-] mseI alwI[dam-] bstXI/xhoII ahaIII/draI bfaI mboII[dam-] TTTAAAAGGA TCTAGGTGAA GATCCTTTTT GATAAT AAATTTTCCT AGATCCACTT CTAGGAAAAA CTATTA
maell BCACCACCACG CCA CTGTGGTGC	I acli mnli rgg AggcggaTA Acc TccgccTAT		ddel nlalv mbol/ndell[dam-] dpnl[dam+] hglCl dpnll[dam-] banl i GATCGCT GAGATAGGTG	rmal mael sal mael sal sau3Al hphl mb mbol/ndell(dam-) dpnl(dam+) dpi dpnli(dam-) dpi tru9l bstrl/xholl al msel alwl(dam-) bstr ahalll/dral bfal mboll() tTTAAAAGGA TCTAGGTGAA GA AAATTTCCT AGATCCACTT CT
6601 CGACGAGC GCTGCTCC	fokI bsri 6701 GACTGGAT CTGACCTA	acil thal thall/m\ batul batul 6801 CTCGCGGTAT GAGCGCCATA	Bau3AI Bau3AI mbol/n dpnI[d dpnII[ 6901 ACAGATCGCG TGTCTAGCG	tru91   msel   ehall/

nI cac8! dpn[[dam+] fnu4HI acil n8pBII hpaII aluI cbbvI crgcrgcttg caaacaaaa aaccaccca accacgcg gttgttgttgt	haelli/pali bsli hael TAGCCGTAGT TAGGCCACCA CTTCAAGAAC ATCGGCATCA ATCCGGTGGT GAAGTTCTTG	scrFI ncil mspI hpalI dsav pleI caulI hinfI CGCGATAAGT CGTGTCTTAC CGGGTTGGAC TCAAGACGAT	nacii napBli bacil fuudHi bacil286 bacil2866 bacil28666 bacil28666 bacil286666 bacil2866666 bacil286666666 bacil286666666 bacil286666666666 bacil28666666666666666666666666666666666666
acii acii nspbli ACCACGCI ACCAGGG	rmal haeIII/pa mael bsli haeI calatactet cettetagig tagecetaer tageceaeca gittatgaea ggaagateae ateegeteet	GCGATAAGT CGTGTC	SGAGCGAAC GACCTA
BI TG CAAACAAAAA AA TG CTTTGTTTTT TJ		fnu4HI bsoFI bbvI fnu4HI alwNI[dcm-] srI bsoFI bbvI bsrI cAGTGGC TGCTGCCAGT G	hgial/aspHi bspl286 bsiHKAI bmyl apaLi/snoi alw441/snoi alw45CCCAGCT TC
_	hinPI 71 hhal/cfol AGCAGA GCGCAGATAC FCGTCT CGCGTCTATG	alwni beri maelii TCCTGT TACCAGTG	hglAl/as bspl286 bslHKAI bmyl apaLl/sn alw441/s GAACGGGGG TTCGTGCACA
an-) h h TC TG	bsrl maelil eco571 7201 GCTACCAACT CTTTTCCGA AGGTAACTGG CTTCAGCAGA CGATGGTTGA GAAAAAGGCT TCCATTGACC GAAGTCGTCT	fnu4HI bsoFI bbvI fnu4HI fnu4HI alwNI[dcm-] bsrI bsoFI naeIII bbvI bsrI nagCAC CGCCTACATA CCTCGCTCTG TACCAGTGC TGCTGCCAGT AGACATCGTG GCGGATGTAT GGAGCGAGA GATTAGGACA ATGGTCACCG ACGACGGTCA	acii pBII (4HI FI mcri I mcri cfoi cGTCGGGCT GAAC
mboll[dam-] sau3Al mbol/ndell[d mbol/ndell[dam-] dpnl[dam+] dpnl[dam+] dpnl[dam+] betxl/xholl alwl[dam-] alwl[dam-] betxl/xholl Alwl[dam-] Agril/xholl Alwl[dam-] Agril/xholl AGTITCCTAG AAGAACTCTA GGAAAAAAA	ACT CTTTTCCGA TGA GAAAAGGCT	acil cac cecctacata cte ececatata	acil napli finutti hpali baoFi sawi hinPl bsiEi II hhal/cfoi CCGGA TAAGGCGCAG CGGTCGGCT GGCCT ATTCGGGTC GCCAGCCGA
s m d d bs s1 7101 TCAAAGG	7201 GCTACCA CGATGGT	BCfI 7301 TCTGTAG AGACATC	mspi hpaii bsawi maeiii 7401 AGTTACCGGA

### FIG. 48W

BCLFI mvaI

Н. вн≚			
eccRII deav betNI beaJI aluI apyI[dcm+] ccTCGAAGGT	nlalv :11 :GG AGCCTATGGA	TGGATAACCG ACCTATTGGC	
bessi hinPi mnli hhal/cfoi AccccAccAc	nla acii AGGGGGGGG TCCCCCGGC	tf11 h1nf1 ccrgartcrg ggactaagac	
GGAACAGGAG	efani Gatgetegte Ctaegageag	TGCGTTATCC	
mspl hinpi hhal/cfol haeli haeli tGAGCATTGA GAAAAGGGCT CCCTCTTTC CGCCTGTCCA TAGGCCATTC GCCTCCCAG CCTTGCTCC CCTCCTCTCC CCTCCAAGGT  mspl haeli haeli haeli haeli cctcctcttcccAGGT ATCCGGTAAG CGCCAGGGTC GGAACAGGAG AGCGCACGAG GGAGCTTCCAAGGT ACTCGTAACT CTTTCGCGGT TCCCTCTTTC CGCCTGTCCA TAGGCCATTC GCCGTCCCAG CCTTGTCCTC TCGCGTGCTC CCTCGAAGGT	scrFI mval ecoRII dsaV bstNI apyl[dcm+] apyl[dcm+] ccccrrrc ccrcrrc ccccrrcc ccraaaaca crccccc rccaccrrcc rcccccccc	haeIII/pali haeIII/pali fnu4HI scrFI backi mval bsli acti dcav thal bsli dsav fnuDII/mvni apyl[dcm+] haeIII/pali nspli bstlii nlaiv haeI cac8I aflili AAAACGCCAG CAACGCGCC TTTTACGCT TCCTGGCCTT TTGCTGGCTT TGCTGGCTT ACAAGAAAGG ACGCAATAGG GGACTAAGC TTTTGCGGTC GTTGCGCCG AAAATGCCGAA AACGACCGGA AAACGAGTGT ACAAGAAAAGG ACGCAATAAGC GCACTAATTGCC	
mspi hpaii fr bsli be bsawi ac ATCCGGTAAG	tedi hgai ACTTGAGCGT TGAACTCGCA	nlaili haeili/pali nspi aei nsphi 81 · aflili GGCCT TTTGCTCACA TG	
acii GCGGACAGGT CGCCTGTCCA	mnli drdi GCCACCTCTG ACT CGGTGGAGAC TGA	/pall haell cac8l TTGCTGGCCT AACGACCGGA	4
AGGGAGAAAG	GTCGGGTTTC	haeIII/palI scrFI mvaI bslI ecoRII dsav bstNI apyI[dcm+] laIV haeI ca GGT TCCTGGCCTT TTGC	7
fol CGCTTCCCGA GCGAAGGGCT	TTATAGTCCT	haelii/pali u4Hi ofi 11 1 bali Dii/mvni UI 12361 nla GGCC TTTTTACGGT	
hinPi hhal/cfol haeli GAAAGCGCCA CG	scrFI mvaI ecoRII dsav bstNI apyI[dcm+] cCTGGTATCT	haeIII/P fnu4HI bsoFI acil thai bslI fnuDII/mvnI bstUI bshl236I CAACGCGCC TTT	
mapl hinPI hhal/cfol hael haeli haeli 7501 TGAGCATTGA GAACAGGG GGAACAGGT TCCCTTTC CCCTGTCA TAGGCCATTC AGGCACGAC GCCTCCTCTTTC CCCTGTAAGGT TAGCCATTC AGCGAAGGT CCTCGAAGGT AGCCGAAGGT AGCCAAGGT AGCCCAAGGA AGCCCACCACGA GGAGCTTTCCAAGGT AAGCCCAACGA AGCCCAACGA GCAACAGGT AAGCCAACCAAGGT AAGCCCATTC GCCGTAACT TCCCTTTTC CCCCTGTAAGT TAGCCCATTC GCCGTCCCAG CCTTGTCCTC TCCCGTGCTC CCTCGAAGGT	scrFI mval ecoRII dsav bstNI apyI[dcm+] mpli drdI hgal apyI[dcm+] ccccTTTGC GGACCTATGGA CGGTGGAGAC TGAACTCGCA GCTAAAAACA CTACGAGAGCAG TCCCCCCGC TCGGATACCT	haeIII/pali haeIII/pali fnu4HI scrFI bsoFI mval bsli acii ecoRII thal bsli dsaV fnuDII/mvnI bstVI haeIII/pall nspli bstU1 napHI haeI cac8I aflIII  7701 AAAACGCCAG CAAAAATGCCA AGACCGGAA AACGACTGA AAACAGAAAAGG ACGCAATAAGG GACTAAAGA ACCTATTGCCT TTTTCCGCCG AAAAATGCAA AGAACGGAA AACGACGGA AAACGAGAAAAGG ACGCAATAAGG GACTAAAGA ACCTATTGCCGTC TTTTCCGCCGG AAAAATGCAA AAGAACGGGA AAACGAGGAAAAAGGA AAAAATGCAA AAAAATGCAA AAAAATGCAA AAAAATGCAA AAAAATGCAA AAAAAAAGAAAAAGGAAAAAGGAAAAAGGAAAAAAGAAAA	
7501	7601	7701	

bbvI baoFI baoFI baoFI baoFI mcrI hinPI bbvI pleI mcII hhal/cfoI barBI fnu4HI mcII hinPI hinFI hinFI hinFI aciI baoFI baiEI hhal/cfoI mnlI aciI haeII haeII hartaccacc TTTGAGTGAG CTGATACCACC GAACGACCAC GAACGAGGAGGGG AAGAGCACCAAA ATACCCAAA ATACCACC TTTGACTACTC GACTATGCGCG CTGATGCCGC CTTGCCGCG TTATGCGTTT ATATGCCGC TTCTCGCGGG TTATGCGTTT

fnu4HI

bsoFI bbvI

```
maeIII
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       hhal/cfol asel/asnl/vspl
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            acii acii hhal/cfoi asel/asnl/vspi ceccercre eccentre fectande for the cecercre eccentre fectandes fectandes fectandes fectandes fectandes fectandes from the fectandes fectandes from the fectandes from the fectandes for the fectandes for the fectandes from the fectandes for fectandes from the fectandes for fectandes from the fetandes from 
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        mseI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              hinPI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              cacel
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       cac8I
aluI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              eael tfil asel/asnl/vspl
cfrl hinfl msel nspBil
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Iluvq
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    tru9I
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             bstUI haeIII/pall bsh12361
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  ecoRII
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            scrFI
                                                         fnuDII/mvnI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        dsav
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       mval
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             fnuDII/mvnI
                                                                                                                                                                                                                      Deh1236I
                                                                                                                                                                                                                                                                                                                                                                            hhaI/cfoI
                                                                                                                                                bstul
thaI
                                                                                                                                                                                                                                                                                                       hinPI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     belI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     mnlI
```

FIG. 48Y

8001 ACCTCACTCA TTAGGCACCC CAGGCTTTAC ACTTTATGCT TCCGGCTCGT ATGTTGTGG GAATTGTGAG CGGATAACAA TTTCACACAG GAAACAGCTA TGGAGTGAGT AATCCGTGGG GTCCGAAATG TGAAATACGA AGGCCGAGCA TACAACACAC CTTAACACTC GCCTATTGTT AAAGTGTGTC CTTTGTCGAT

mspI hpall

hgici apyi [dcm+]

banI beaJI

nlaIV bstNI

acil barBi

asel/asnl/vspl

8101 TGACCATGAT TACGAATTAA

nlalII

xmnI asp700

tru9I

msel

```
3167 3179 3188 3200 3210 3221 3267 3372 3404 3449 3686 3949 4021 4318 4542 4727 4739 4748 4760 4770 4781 4827 4910 4914 5070 5127 5153 5166 5203 5217 5220 5248 5275 5680 5699 5741 5751 5790 5979 6026 6125 6234 6311 6355 6476 6522 6713 6804 7166 7175 7310 7420 7541 7560 7687 7715 7806 7827 7834 7877 7901 7911 7967 8070
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  5 44 332 386 390 753 1097 1165 1370 1431 1951 2603 2751 2784 3282 3336 3340 3562 3566 3676 3733 3792 4270 4288 4311 4344 4554 4842 4896 4954 5047 5333 5590 5803 5822 6516 6579 6679 7200 7457 7593 7819 7937 8096
                                                                                                                                                                                       823 1039 2738 4237
217 229 238 250 260 271 317 422 454 485 574 1385 1795 1871 2248 2250 2758 2982
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               988 1690 1858 5117 5947 6329
696 4935 6290 6982 7001
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         1876 5651 6198 7444
                                                                                                                                                            2969 3967 4529
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          ahdi/eam11051(GACNNNNGTC): 2087 6865
                                                                                                                                                                                                                                                                                                                                                                                see hinli
786
                                                                                                                                                                                                                                                                                                                                                                                                                                             932 7758
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                1833
ACTGGTACTA ATGCTTAATT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               ahali/beaHI (GRCGYC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  ahalli/dral(TTTAAA):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           alw44I/snoI(GTGCAC):
                                                                                                                                                                                                                                                                                                                                                                                                                     aflii/bfri(CTTAAG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                aflii(ACRYGT):
                                                                                                                                                            acc651 (GGTACC):
                                                                                                                               aatii(GACGTC):
                                                               >length: 8120
                                                                                                                                                                                              accI (GTMKAC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       ageI (ACCGGT):
                                                                                                                                                                                                                                acil(CCCC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 aluI (AGCT):
```

FIG. 48Z

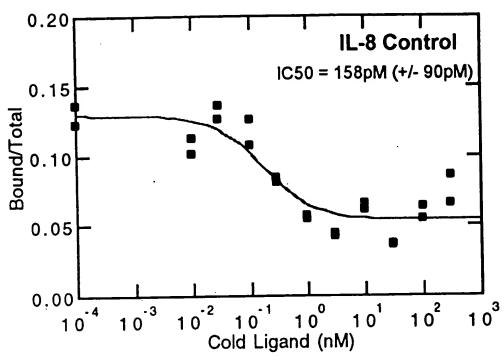


FIG. 49A

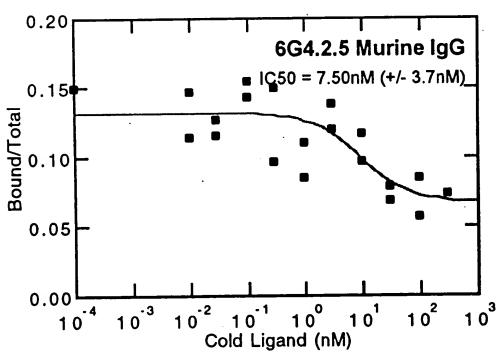


FIG. 49B

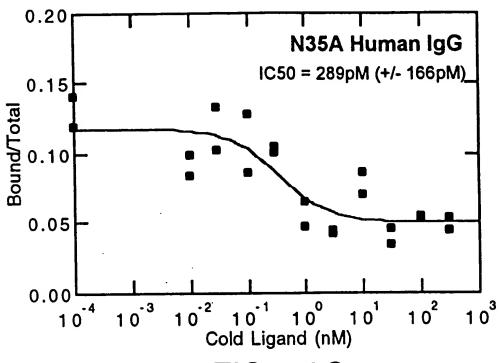


FIG. 49C

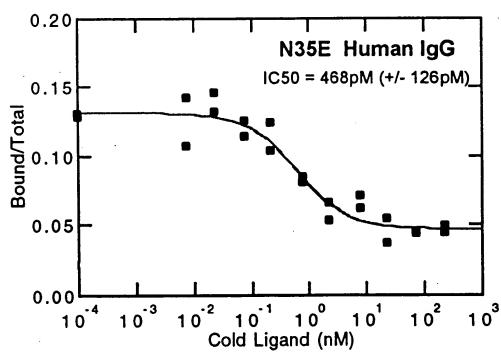
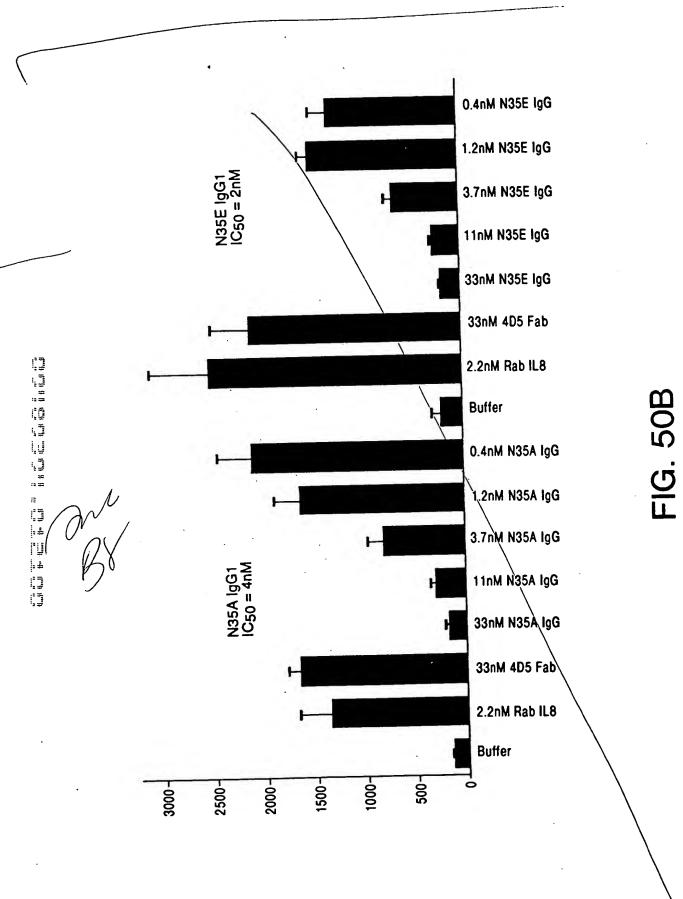
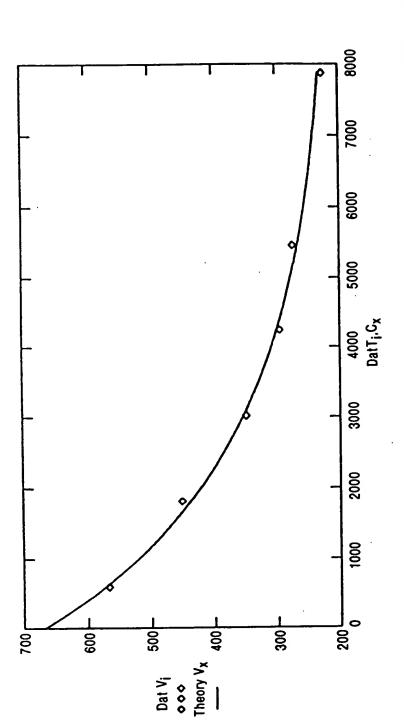


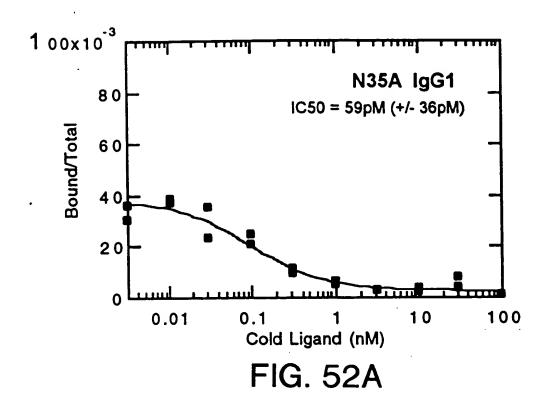
FIG. 49D





Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.IgG1

ſ		  FIG. 5		
Kd	350pM	88pM	49pM	
kd	2.9×10 <sup>-4</sup>	$7.7x10^{-5}$	1.4x10 <sup>-4</sup>	
ka	8.3×10 <sup>5</sup>	8.7×10 <sup>5</sup>	3.0x10 <sup>6</sup>	
SAMPLE	Murine 6G4.2.5 IgG2a	6G4V11N35A-IgG1	6G4V11N35E-IgG1	



N35E IgG1

80

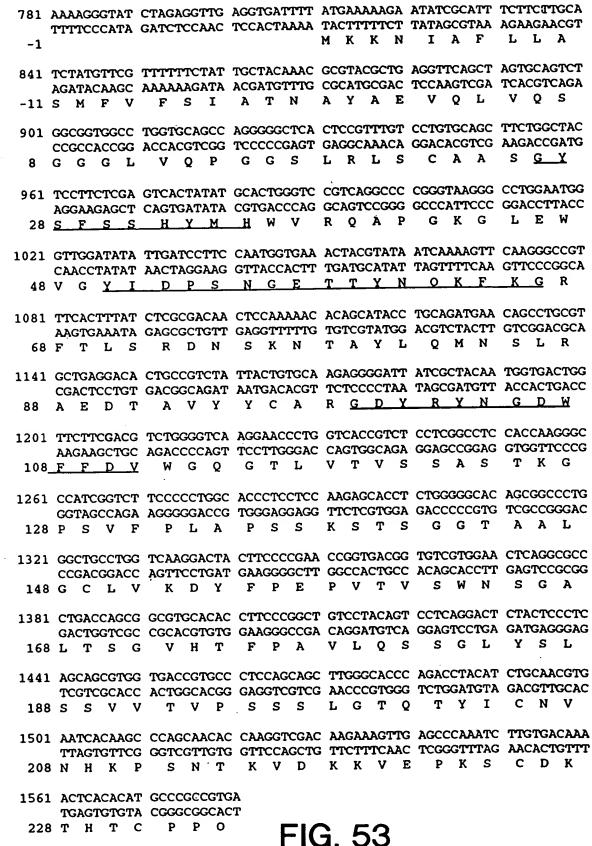
IC50 = 19pM (+/- 15pM)

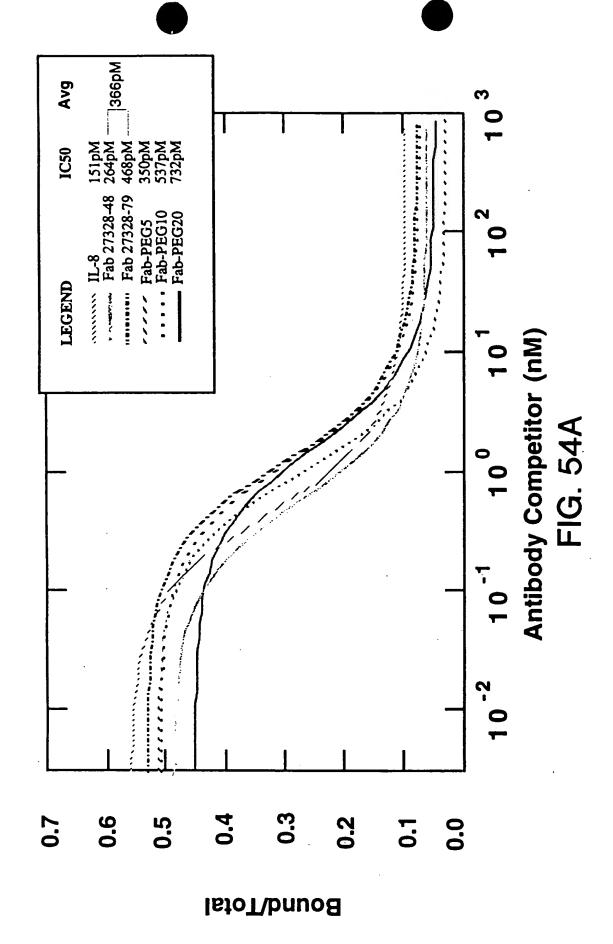
0.01

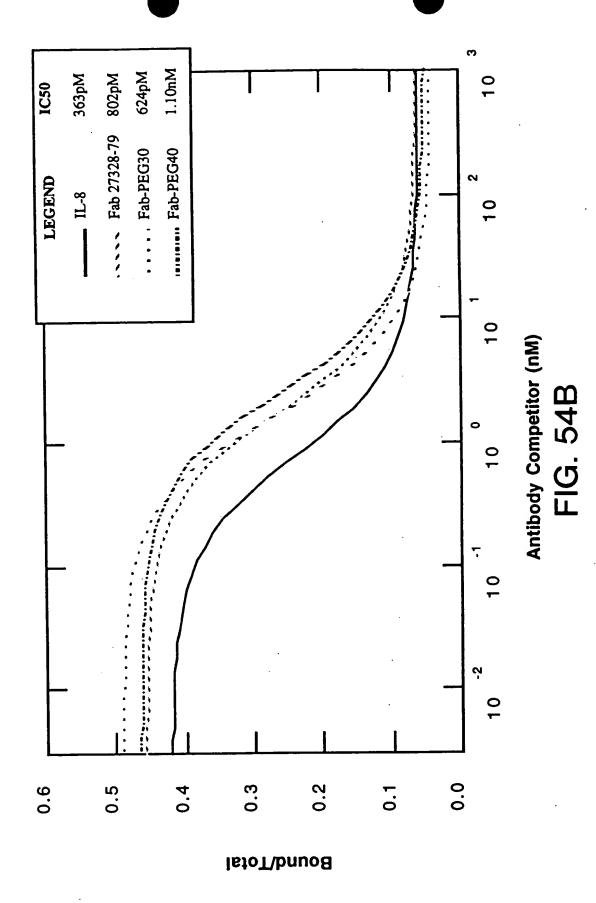
0.1

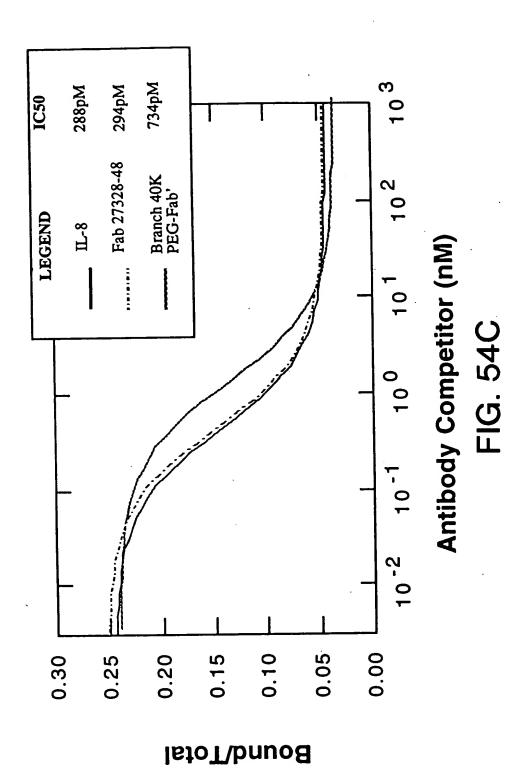
Cold Ligand (nM)

FIG. 52B









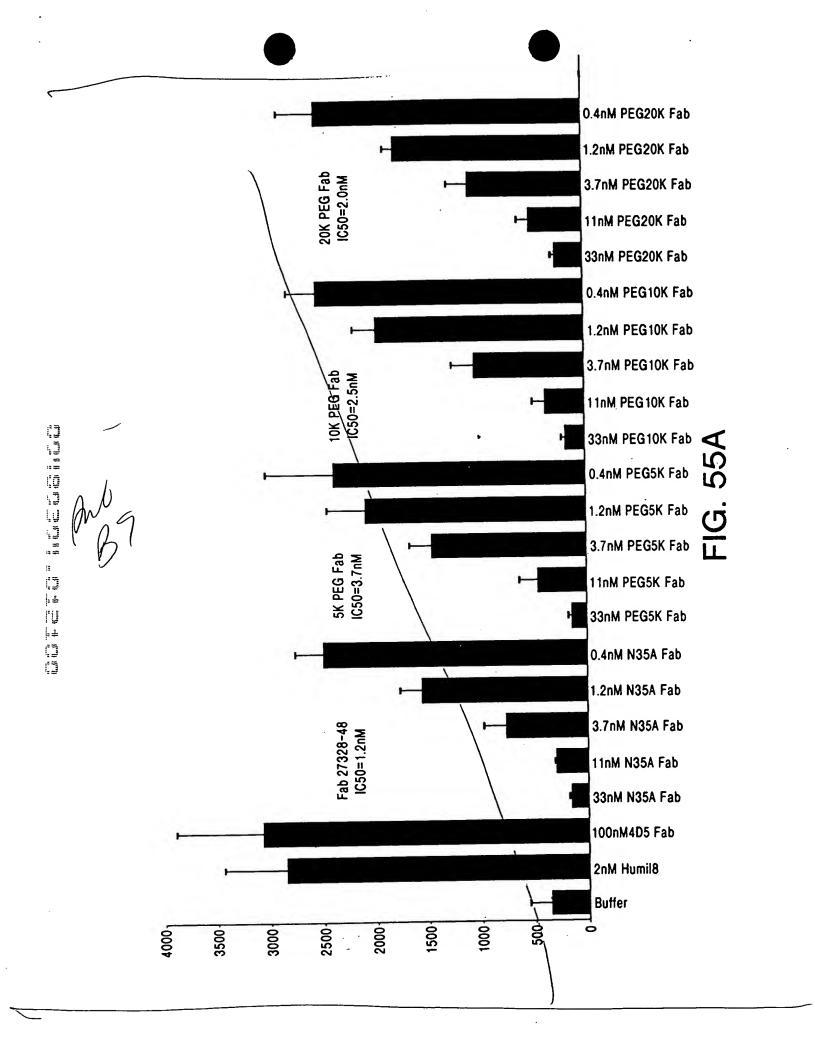
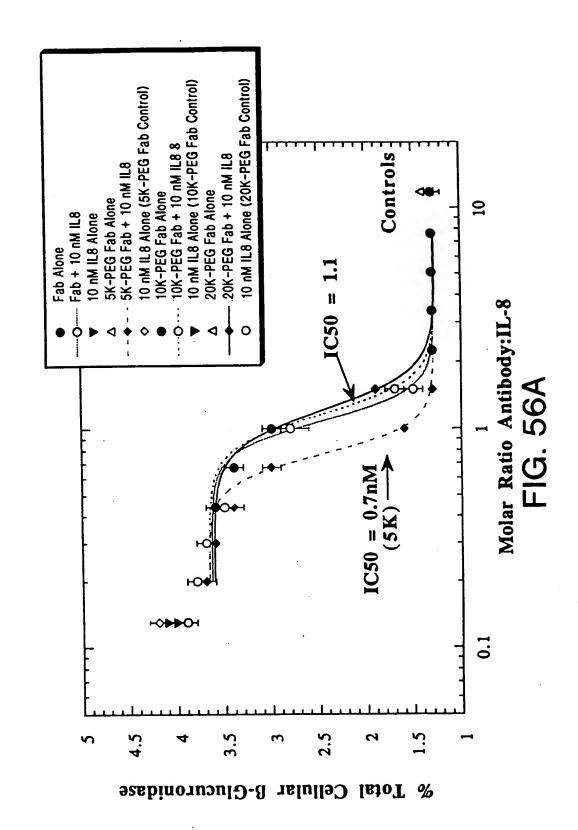
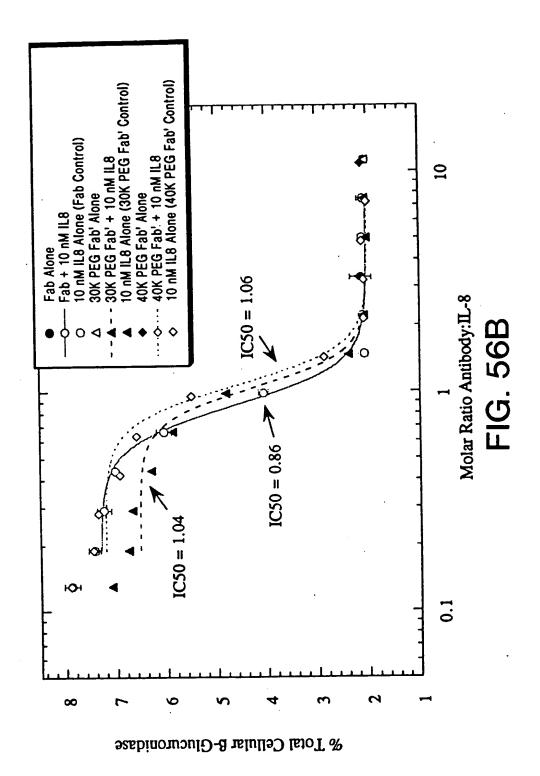


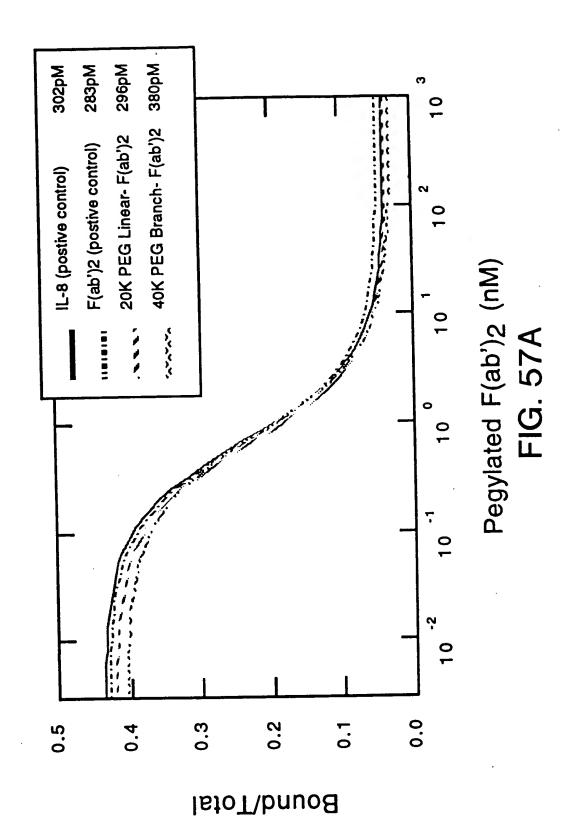
FIG. 55C

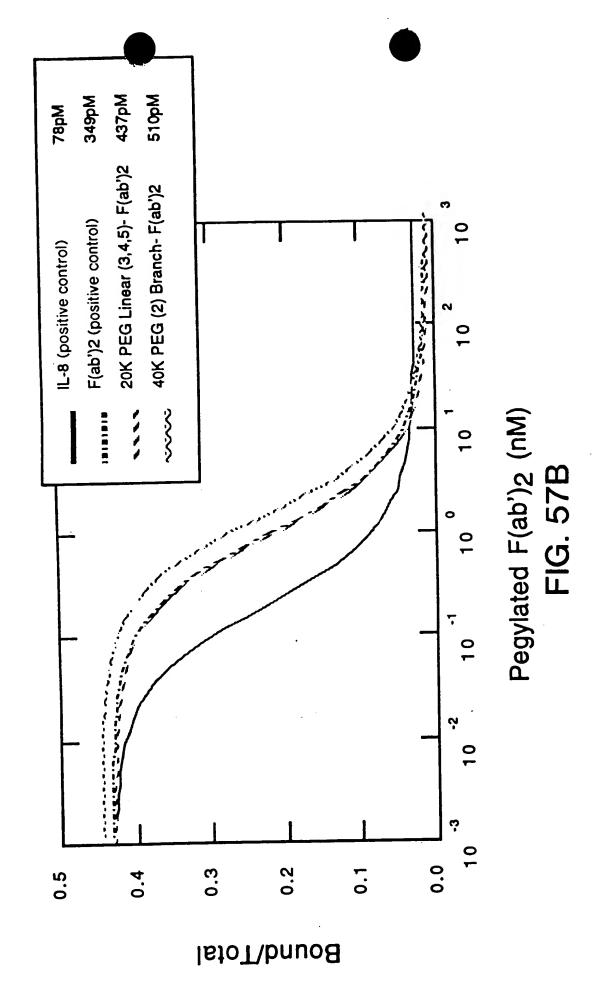


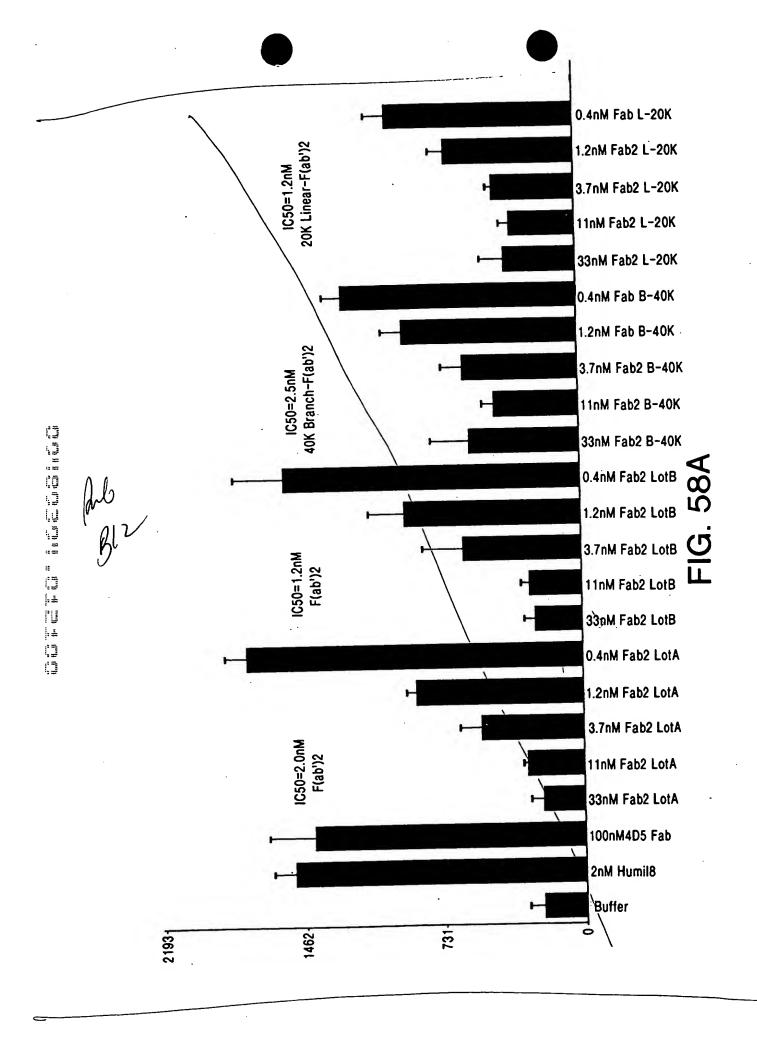


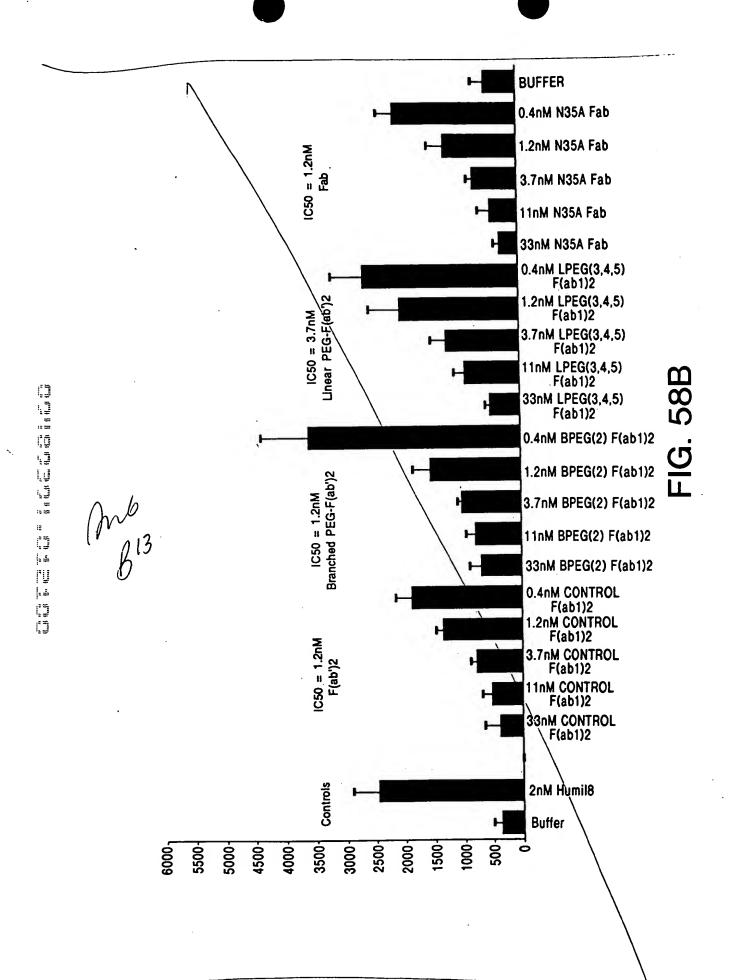
IL8 Alone (40K Br PEG Fab' Control) 40K Branched PEG Fab' IC50 = 1.144 - 40K Br PEG Fab' + 10 nM IL8 2 40K Br PEG Fab' Alone IL8 Alone (Fab Control) · Fab + 10 nM IL8 Fab Alone Molar Ratio Antibody: IL8 FIG. 56C Fab Control IC50 = 0.8320.1 9

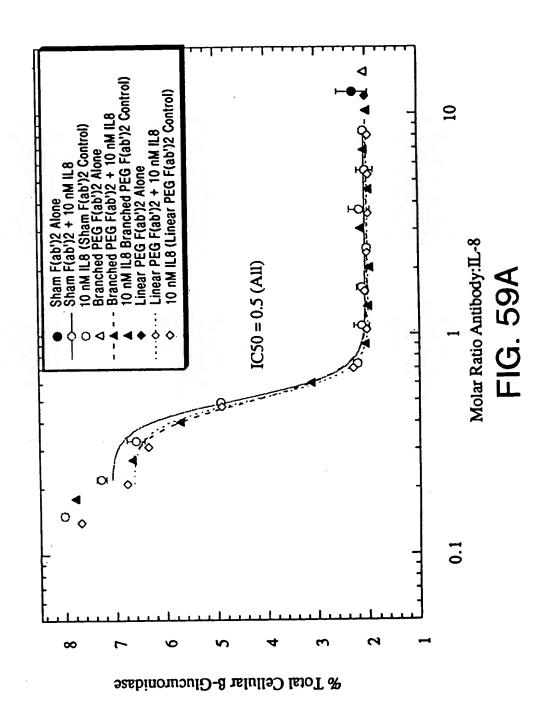
% Total Cellular B-Glucuronidase Activity

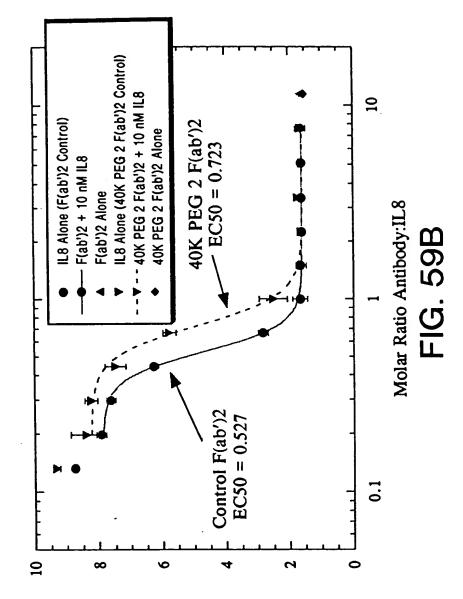




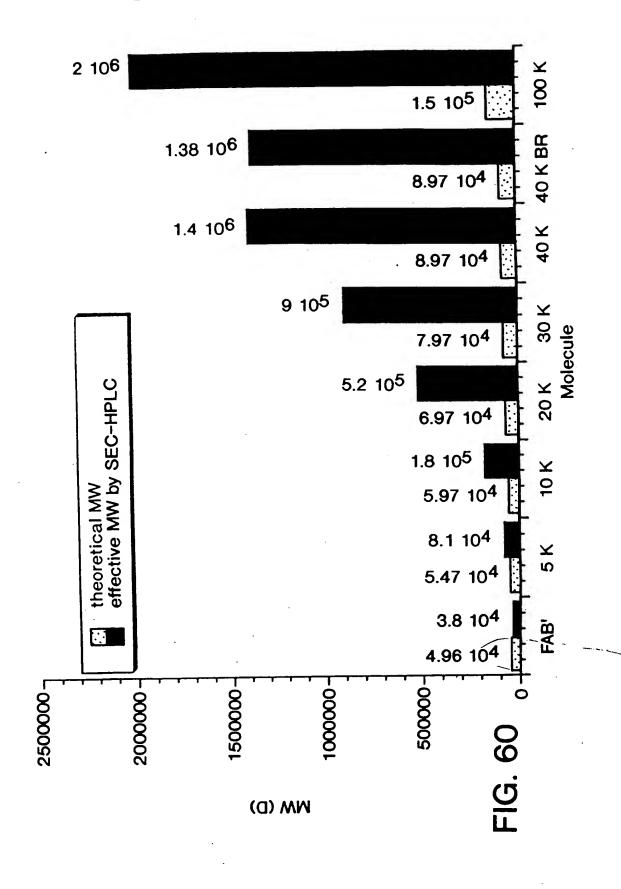


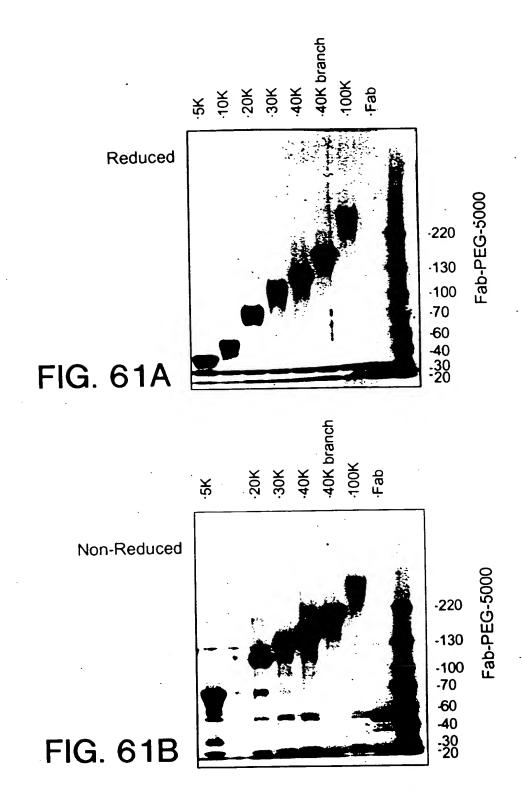


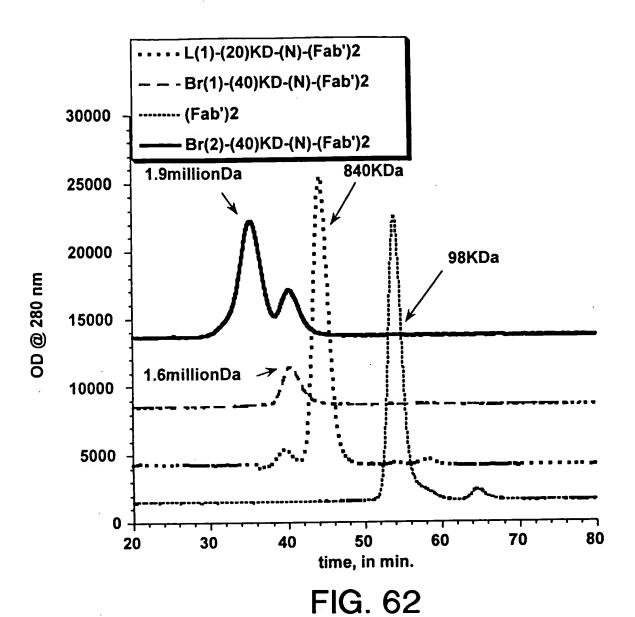




% Total Cellular B-Glucuronidase Activity







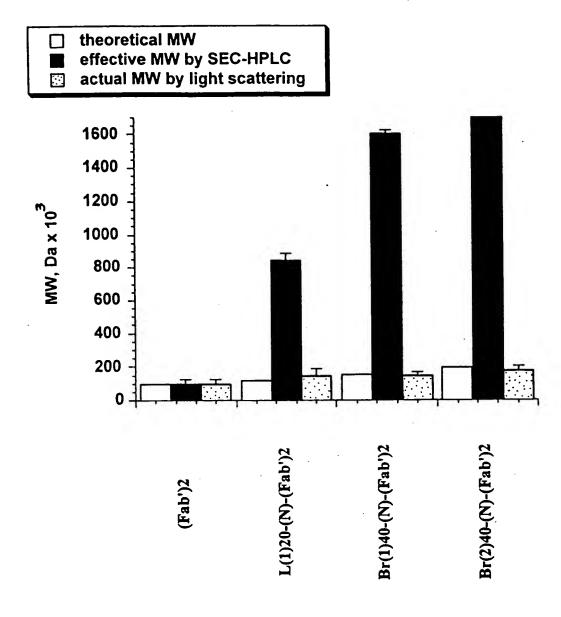


FIG. 63

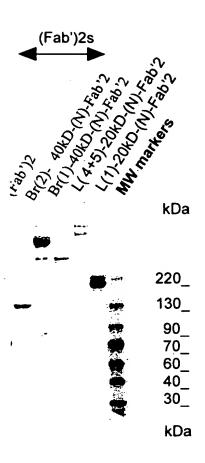
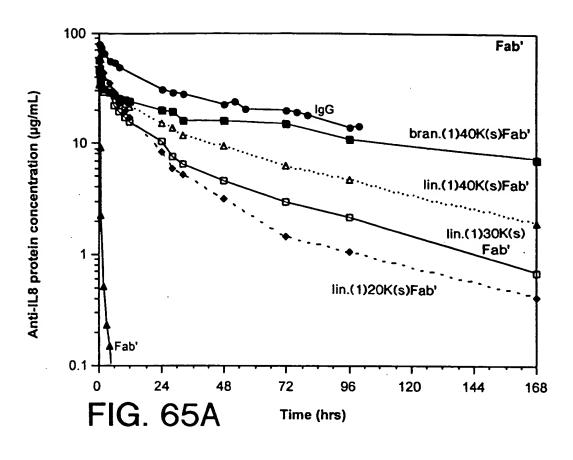
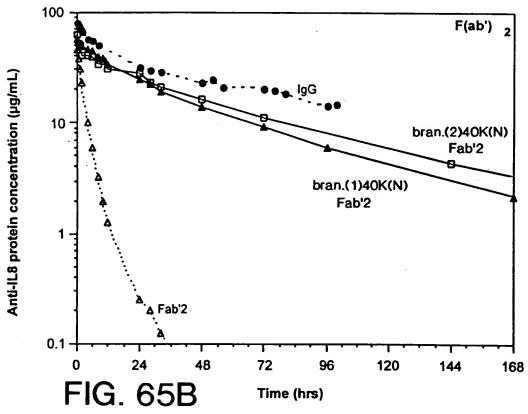


FIG. 64





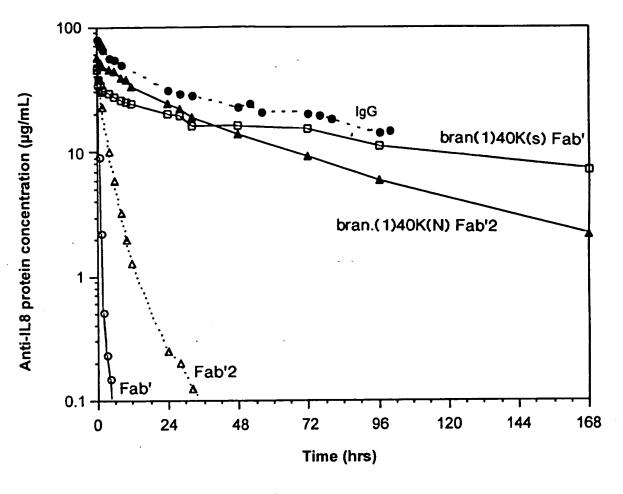
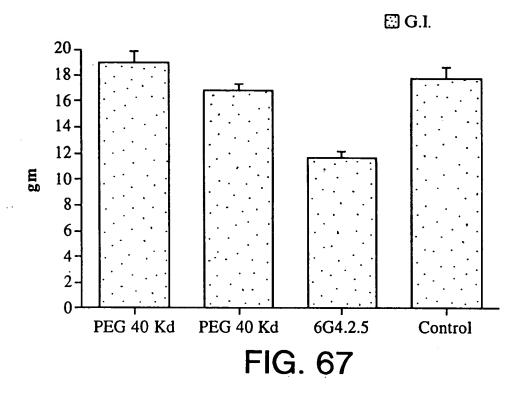
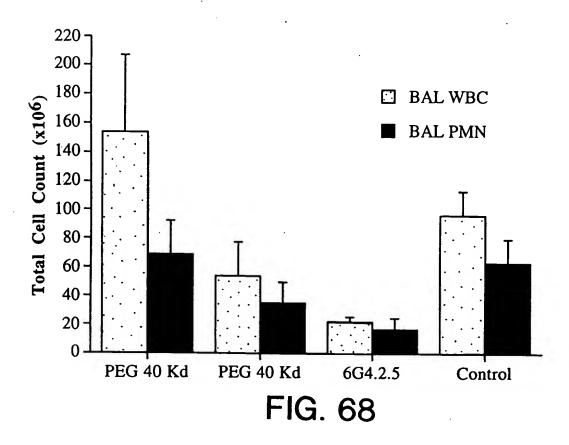
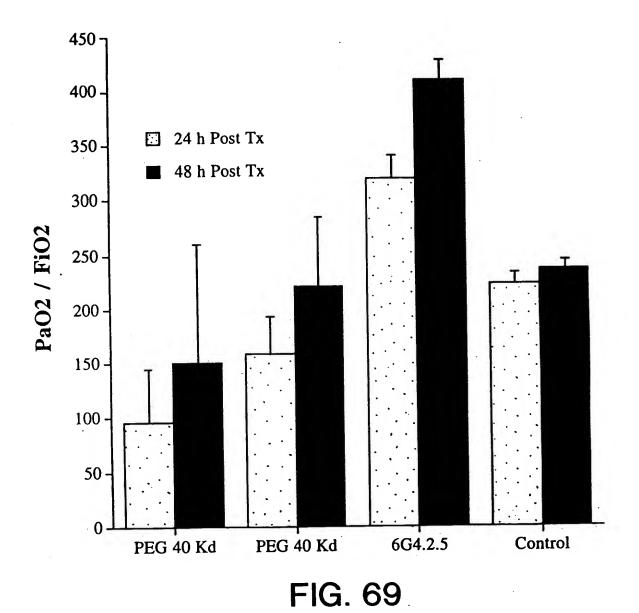
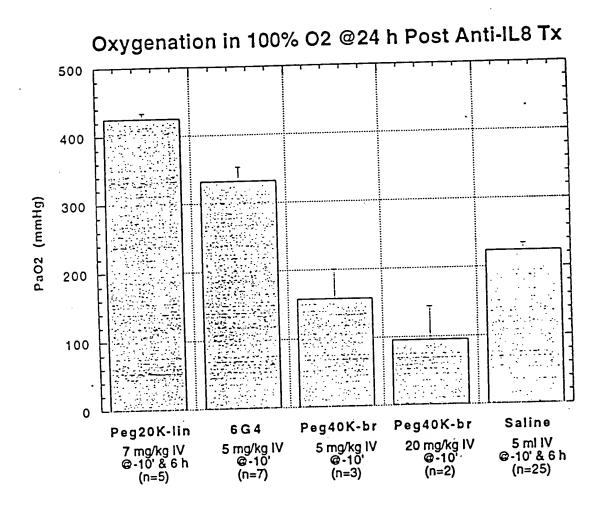


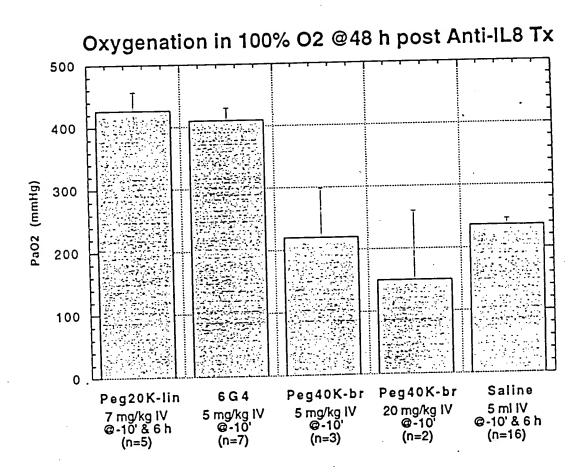
FIG. 66

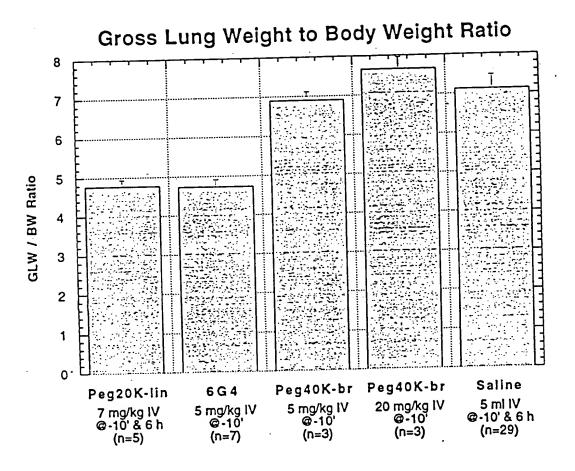




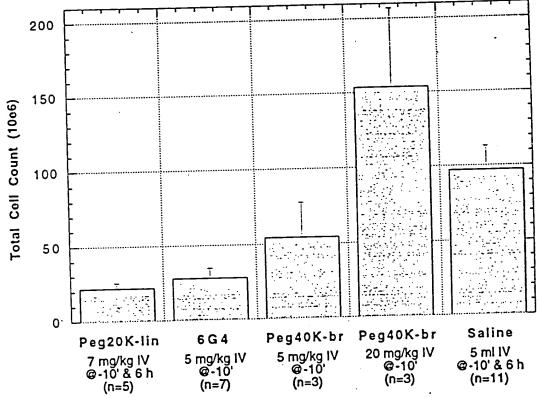


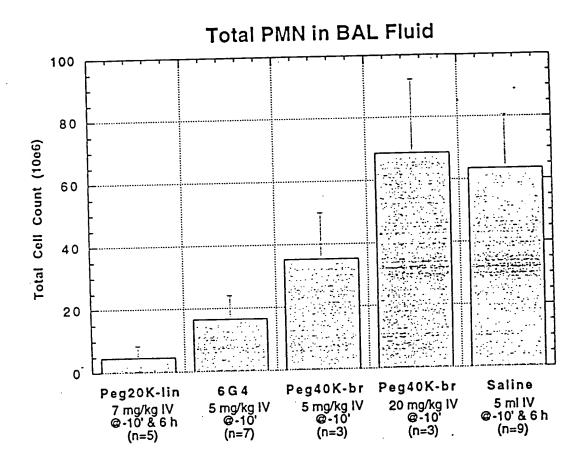




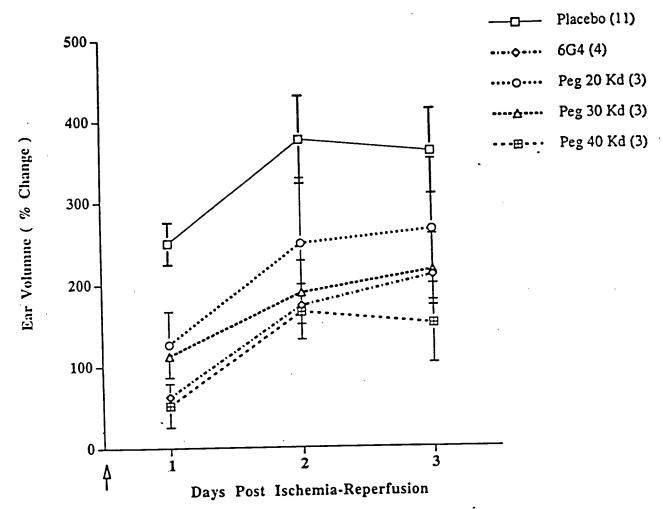


## Total WBC in BAL Fluid

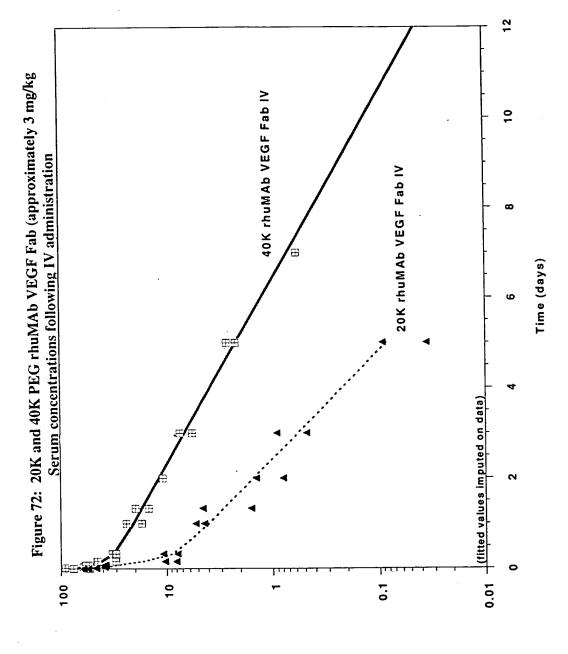




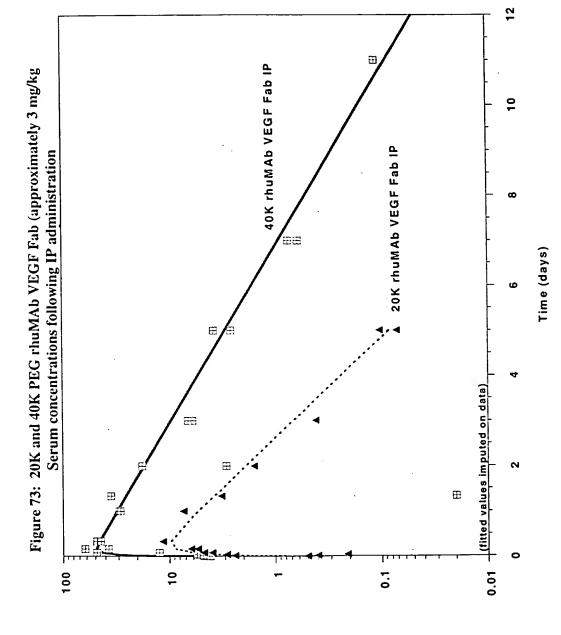
## The Effect of Pegylated Anti-IL-8 in the Rabbit Ear model of Ischemia-Reperfusion Injury



Anti-IL-8 formulations: Single Dose (5 mg/kg) administered IV at time of reperfusion



Serum Concentrations (ug/mL)



Serum Concentrations (ug/mL)

## TUMOR WEIGHTS AT NECROPSY 98-277

